# THE MEDICAL JOURNAL OF AUSTRALIA

VOL. I.—44TH YEAR SYDNEY, SATURDAY, JUNE 29, 1957 No. 26

## Table of Contents.

[The Whole of the Literary Matter in THE MEDICAL JOURNAL OF AUSTRALIA is Copyright.]

**ORIGINAL ARTICLES—** Page

Listerian Oration—Developments in Heart Surgery, by C. J. Officer Brown .. .. .. .. .. .. .. 897

The L.E. Phenomenon in Rheumatoid Arthritis, by the late L. J. A. Parr, Eva A. Shipton, Philip Benjamin and Paul H. H. White .. .. .. .. 900

The Significance of the L.E. Cell Test, by D. C. Cowling, M.D., M.R.A.C.P., M.C.P.A., and I. D. Thomas, M.B., B.S. .. .. .. .. .. .. .. 905

Investigation of Amino Aciduria in Erythroblastosis Fœtalis and its Possible Relationship to Kernicterus, by P. J. Nestel, M.R.A.C.P., and Lydia Nestel, B.Sc. .. .. .. .. .. .. .. 909

**REPORTS OF CASES—**

A Contribution to the Study of Collagen Disease and the L.E. Phenomenon, by Eva A. Shipton 911

**REVIEWS—**

The Essentials of Modern Surgery .. .. .. .. 915

A Companion in Surgical Studies .. .. .. .. 916

**BOOKS RECEIVED** .. .. .. .. .. .. .. .. .. 916

**LEADING ARTICLES—**

Road Accidents as a Medical Problem .. .. .. 917

**CURRENT COMMENT—**

Intravascular Clotting .. .. .. .. .. .. .. 918

Dr. Samuel Adams and His Diary .. .. .. .. 919

Soviet Invitations .. .. .. .. .. .. .. 920

A Follow-Up Study of Frontal Lobotomy .. .. .. 921

**ABSTRACTS FROM MEDICAL LITERATURE—**

Dermatology .. .. .. .. .. .. .. .. .. 922

Urology .. .. .. .. .. .. .. .. .. .. 922

**BRITISH MEDICAL ASSOCIATION NEWS—** Page

Scientific .. .. .. .. .. .. .. .. .. .. 924

**PUBLIC HEALTH—**

The Influenza Epidemic in the Far East .. .. .. 929

**OUT OF THE PAST** .. .. .. .. .. .. .. .. .. 930

**CORRESPONDENCE—**

The New South Wales Medical Register .. .. .. 930

The Good Life .. .. .. .. .. .. .. .. 930

**POST-GRADUATE WORK—**

The Post-Graduate Committee in Medicine in the University of Sydney .. .. .. .. .. .. 931

**DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA** .. .. .. .. .. .. 931

**AUSTRALIAN MEDICAL BOARD PROCEEDINGS—**

Queensland .. .. .. .. .. .. .. .. .. 932

Tasmania .. .. .. .. .. .. .. .. .. .. 932

**CORRIGENDUM** .. .. .. .. .. .. .. .. .. 932

**NOMINATIONS AND ELECTIONS** .. .. .. .. .. 932

**HONOURS—**

Corrigendum .. .. .. .. .. .. .. .. .. 932

**DEATHS** .. .. .. .. .. .. .. .. .. .. 932

**DIARY FOR THE MONTH** .. .. .. .. .. .. .. 932

**MEDICAL APPOINTMENTS: IMPORTANT NOTICE** .. 932

**EDITORIAL NOTICES** .. .. .. .. .. .. .. .. 932

## Listerian Oration.[1]

### DEVELOPMENTS IN HEART SURGERY.

By C. J. OFFICER BROWN,
*Alfred Hospital, Melbourne.*

WE have come together tonight to honour the greatest man that medical science has known. Lord Moynihan said: "If services to mankind are the standard of a man's greatness, Lister was the greatest the world has known, first among material benefactors of mankind."

Lister had no telephone and no car, little or no laboratory help and, indeed, little in the way of a laboratory. Without typewriters or tape-recorders, everything had to be written painstakingly in longhand. Today, without these time-savers we should be lost. Yet, his researches were legion and epoch-making, and his literary output was prodigious.

Imagine what might have happened if the order of scientific discoveries had been different. What would have been the toll of our roads if the internal combustion engine had been invented and applied before the genius of Pasteur and Lister had shown us how to master the infections of earlier days? We shudder to think of the prospects of a deliberately controlled germ warfare; but the uncontrolled effect of germs would surely have made modern mechanical warfare impossible if Lister had not lived. Imagine the horror of an air raid on London with surgery in the pre-Listerian phase.

Lister enjoyed his work and found pleasure in seeking answers to unsolved problems. He worked on the frontiers of surgical knowledge, and tonight I propose to review briefly some pioneering work in heart surgery and particularly the things that are coming: methods that we know will work, that have been made to work in a few centres, but are still in the pioneering stage, with much labour and heart-burning and many failures still to come; methods that are being developed by many hundreds of devoted workers, with every advantage that modern science can provide, but, nevertheless, imbued with the passion for truth that illuminated all that Lister did.

Just over eighteen years ago, in 1938, Gross of Boston successfully ligated a patent *ductus arteriosus*, and this may be looked upon as the birth of modern heart surgery. Although in the same year E. S. J. King, now Professor of Pathology in Melbourne, was able to write a Jacksonian Prize Essay on the surgery of the heart, which he later published as a book of 700 pages, it is fair to say that, up to that time, heart surgery had hardly advanced beyond the pericardium. Since then it has become a major specialty, and especially in the last ten years has been the most active and exciting field of surgical advance.

[1] Delivered at a meeting of the South Australian Branch of the British Medical Association on March 28, 1957.

The operations performed by heart surgeons fall naturally into a few groups. First, there are those performed on the great vessels close to the heart—closure of a patent *ductus arteriosus*, resection of a coarctation of the aorta, shunt operations for Fallot's tetralogy and the division of congenital vascular rings. These operations are really extracardiac and are based on simple principles of surgical technique; the first two are amongst the most perfect operations in surgery, because they remove a defect, restoring conditions to normal and adding many years to the life expectancy of the patient. The mortality rate for closure or division of a patent *ductus arteriosus* in skilled hands is a fraction of 1%, and for resection of a coarctation it is about 5%; this mortality is largely a consequence of associated conditions and complications existing before surgery is considered.

The principle of shunting blood from the systemic circulation into the pulmonary artery to improve exercise tolerance and overcome cyanosis in Fallot's tetralogy was introduced by Blalock and Taussig in 1944, and brought happiness to thousands of severely disabled children and their parents. It was known from the start that this operation was palliative and not curative, and now some of these patients are breaking down under the added strain of a large left-to-right shunt. Fortunately, in 1954 Lillihei showed that with open heart surgery both the pulmonary stenosis and the ventricular septal defect could be repaired and the crippled heart virtually restored to normal. As this technique develops and becomes widely practised, shunt operations will be reserved for the few patients whose defect is not suitable for radical cure. Shunt operations have saved many blue babies from invalidism and an early death, and these may soon be offered the prospect of a real cure.

The valves and the septa within the heart can be approached only by true intracardiac techniques; these may be "closed", and performed with an instrument or a finger passed blindly into the heart, or "open", with the flow of blood temporarily arrested. Blind techniques have been successfully applied for the relief of mitral stenosis and pulmonary stenosis, for the closure of atrial septal defects, and, in a few cases, for the removal of foreign bodies or tumours of the auricles. For closure of ventricular septal defects or the radical cure of Fallot's tetralogy, open heart surgery is essential. A closed technique for mitral stenosis may remain the standard operation for some time; but for closure of atrial septal defects and pulmonary valvotomy, there is little doubt that the more precise methods, possible under direct vision, will be preferred as soon as they approach the safety of the closed methods. Stenotic aortic valves are being stretched and split by closed methods, by either the transventricular or the aortic route; but the mortality for these operations is high, and the results are far from encouraging. It is hoped that open methods will give better results in this condition; but McMillan, who has devised a method of making moving pictures of heart valves in action, has shown that, even with the dead heart wide open, it is often impossible to improve the function of these valves.

Table I shows the principal advances that have been made. It is clear that 1938 to 1948 was the period of development of extracardiac operations and that from 1948 to 1953 closed intracardiac operations were developed; 1953 marks the commencement of open heart surgery.

In principle it is obvious that deliberate operating under vision must always be more precise and better adapted to unusual situations, and I believe that open heart surgery is sufficiently developed to enable us to be confident that within the next few years few, if any, intracardiac operations will be performed blindly.

To open the heart, it is necessary to stop the flow of blood through it by occluding the *venæ cavæ*; but the brain will not tolerate circulatory arrest for more than two and a half minutes, and although Varco in 1948 used this period of occlusion to open the pulmonary artery and divide stenotic pulmonary valves, the time is too short for deliberate surgery. The safe period of vascular occlusion may be prolonged either by reducing the body's need for oxygen, as is done with hypothermia, or by providing an alternative circulation.

In 1940, Temple Fay experimented with prolonged chilling in an attempt to control cancer, and although in this he was not successful, he demonstrated that hypothermia was practicable and greatly reduced the demand of the tissues for oxygen. Bigelow and his associates followed up this work, and in 1950 showed that, in experimental animals cooled to about 25° C., the heart could be excluded from the circulation for fifteen minutes, with subsequent recovery. At this temperature the body's demand for oxygen is reduced to about 25% of normal. In 1953, Lewis used hypothermia with circulatory occlusion to open the right atrium and close an atrial septal defect under direct vision. Swan, in Denver, developed a similar technique for open operation on stenotic pulmonary valves, and for these two operations cooling to between 28° and 25° C. has been successfully used in many centres.

TABLE I.

*Development of Cardiac Surgery.*

| Year. | Procedure. | Worker. |
|---|---|---|
| 1938 | Closure of patent *ductus arteriosus*. | Gross. |
| 1944 | Shunt for Fallot's tetralogy. | Blalock. |
| 1945 | Excision of coarctation. | Crafoord, Gross. |
| 1948 | Valvotomy for pulmonary stenosis. | Brock. |
| 1948 | Valvotomy for mitral stenosis. | Bailey, Harken, Brock. |
| 1948 | Closure of atrial septal defect. | Gordon Murray. |
| 1952 | Valvotomy for aortic stenosis. | Bailey. |
| 1953 | Use of plastic valve for aortic regurgitation. | Hufnagel. |
| 1953 | Use of hypothermia for closure of atrial septal defect. | Lewis. |
| 1954 | Use of cross circulation for repair of ventricular septal defect, Fallot's tetralogy and *atrioventriculus communis*. | Lillihei. |
| 1955 | Dog's lung oxygenator for repair of ventricular septal defect, Fallot's tetralogy and *atrioventriculus communis*. | Lillihei. |
| 1955 | Heart-lung machine. | Kirklin. |
| 1955 | Simple disposable artificial oxygenator. | Lillihei. |

The great drawback to hypothermia is ventricular fibrillation, which may come on at any time after cooling is started, and is increasingly likely as the temperature falls. Its incidence is very high at temperatures below 25° C., or when incisions are made into the ventricles. At present these factors limit the use of hypothermia in heart surgery to operations on patients with atrial septal defects or pulmonary stenosis, and on some patients with aortic stenosis.

Hypothermia may be induced by surface cooling with ice, ice water or refrigerated blankets, or by direct cooling of the blood by passing it through a refrigerated coil. Surface cooling has been most generally used, although it is slow and difficult to control. Blood cooling was introduced by Delorme (1952), who joined a superficial femoral artery to a saphenous or femoral vein by nine or 10 feet of refrigerated plastic tube. The blood was pumped through the tube by arterial pressure, and as cooling proceeded, the pressure fell; although the method worked well experimentally, there were disadvantages in applying it to patients with defective hearts. Ross and Brock (1954) developed a system of venous cooling, in which blood was taken from the superior *vena cava* and pumped through a refrigerated coil and back into the inferior *vena cava* via a saphenous vein. Vascular cooling is faster than surface cooling, easier to control and more direct, and it may be applied after the chest has been opened and the need for cooling determined. Brock places the efferent cannulæ in the *venæ cavæ* via the right atrium, and the blood is returned through a cannula previously placed in a saphenous vein.

As cooling proceeds, metabolism is slowed. Oxygen consumption and cardiac output fall. Blood pressure falls and pulse rate diminishes. Respirations diminish in both frequency and amplitude, and artificial respiration is required at temperatures below about 30° C. The clotting time of the blood is increased by cooling and heparin is

not required, even when vascular cooling is used and the blood circulated through plastic tubes outside the body. Serum potassium and sodium and blood sugar levels are not apparently altered. There is a tendency to acidosis, which may be a factor in the increased irritability of the cold myocardium, and adequate ventilation to eliminate carbon dioxide is important in the prevention of ventricular fibrillation.

Ventricular fibrillation remains the chief hazard of hypothermia. Schumaker believes that injection of procaine around the sino-auricular node reduces its incidence, and sympathectomy or the use of sympathetic-blocking agents may be of value. Normal rhythm may be restored by massage and electrical defibrillation, but may be difficult to maintain until the patient has been rewarmed. Brain damage is unlikely to occur in less than ten to fifteen minutes at low temperatures, but nevertheless there is a high death rate when ventricular fibrillation occurs.

Hypothermia has a real place in the management of aneurysms of the cerebral arteries and for some operations requiring prolonged tissue ischæmia, like the resection of thoracic aneurysms. In heart surgery it is satisfactory for open operations for the closure of atrial septal defects and for the relief of pulmonary stenosis; but both these operations can be accomplished with a high degree of success by closed methods. Swan and Brock have used it in operations on aortic stenosis.

Swan is still an ardent advocate of hypothermia, and has recently reported his results in 130 open heart operations performed under hypothermia, with 20 deaths. He believes that the temperature should be kept between 29° and 32° C. (84·2° and 89·6° F.), and that avoidance of lower temperatures will largely eliminate ventricular fibrillation and disturbances of the clotting mechanism. At this temperature he believes that six minutes' occlusion is safe and allows time for operative relief of pulmonary stenosis, atrial septal defects and aortic stenosis, and that the risk of these operations should be less than 5%. He lost only one of the last 30 patients operated upon under hypothermia for these conditions.

Perfusion of the coronary arteries, or of the coronary arteries and the brain, with oxygenated blood as a supplement to hypothermia, is being tried as a method of prolonging the safe period of occlusion and of lessening the tendency to ventricular fibrillation. If cooling is to be of real value in cardiac surgery, some supplement of this type or the safe use of much lower temperatures must be developed. Bigelow holds that the secret may lie in understanding the natural process of hibernation, which occurs in some animals, and is working to elucidate the physiology of this process.

In 1937, Gibbon described a machine to exclude the heart and lungs from the circulation, and since then a vast amount of experimental work has been done and many ingenious pumps and oxygenators have been described to replace the heart and lungs. In 1953, Gibbon successfully repaired an atrial septal defect using a heart-lung machine which he had spent sixteen years developing. This was an isolated success, but has been followed up by Kirklin's work with a similar machine.

The idea of establishing cross-circulation by joining the vascular systems of two animals was suggested by Jacobi in 1890, and in 1952 Southwick and Converse Pierce described a procedure for establishing extracorporeal circulation, in which a donor animal provides the function of the heart and lungs for itself and a recipient whose heart and lungs are excluded. Lillihei and his associates in Minneapolis developed this method, and in 1954 successfully applied it to open heart surgery and carried out 42 operations with 14 deaths. Although all the donors came through the experience unscathed, two of them had close shaves, and because of the risk to the healthy donor, the method was never popular. Following up this success, the Minneapolis team used specially prepared dogs' lungs as the oxygenator in a few cases, and then devised a simple plastic oxygenator, which they have been using with considerable success for the last two years.

While Lillihei was developing cross-circulation, Kirklin and his group at the Mayo Clinic were experimenting with a prototype of the Gibbon machine that had been built in the clinic workshops. In April, 1955, this machine was used with success to close a ventricular septal defect, and since then it has been working satisfactorily. In July, 1956, he reported his experience with 40 operations; 24 patients were living. Many of these patients had been hopelessly ill, and operation was a desperate attempt to save them; 21 were suffering from simple ventricular septal defects, and of these 17 lived and four died; and there was only one death among the last 14 patients operated on for a ventricular septal defect. Fired by the success of these two teams, workers all over the world have redoubled their efforts to make other machines work, or to copy the simple Lillihei oxygenator.

In principle, a heart-lung machine is simple. It must receive venous blood from the *venæ cavæ*, either by gravity or by pumping, and pass it through an oxygenating device, from which it is pumped back into the aorta through a cannulated artery. Passage through the machine must not cause hæmolysis or clotting, oxygenation and removal of carbon dioxide must be adequate, and when the blood is returned to the patient it must be completely free of bubbles, whatever method of oxygenation has been used. Many machines have been built to these specifications and most of them show promise, but so far only Lillihei and his associates and John Kirklin have reported consistent success.

Although the actual operation within the open heart is simple and quick, the amount of surgery required to put the patient on the machine is formidable. The chest is opened with an incision which divides the sternum transversely and opens both pleural cavities widely. The pericardium is opened. The *venæ cavæ* are isolated and surrounded by tapes, and through the right atrial appendage a catheter is passed into each *vena cava*. The right or left subclavian artery is ligated at the apex of the chest and divided, and a catheter is passed through its proximal end into the aorta. A tourniquet is placed loosely around the commencement of the aorta. The machine, already primed with compatible heparinized blood, is connected to the catheters so that blood is taken from the *venæ cavæ* and returned to the aorta. When everything is connected up, the pumps are started. They must be synchronized to prevent overloading or depletion of the circulation. The tapes around the *venæ cavæ* are now tightened around the catheters to stop blood entering the right atrium, and in a few beats the heart has emptied itself and is ready for incision to expose the field of operation. Even now, blood still flows from the bronchial arteries into the lungs and so through the pulmonary veins into the left atrium and through the coronary arteries and coronary sinus into the right atrium, so that the field is not completely bloodless. A sucker is placed in the chamber, which has been opened, to remove this blood and return it to the machine, and for brief periods while a stitch is being placed, the tourniquet around the commencement of the aorta is tightened to stop coronary flow and allow the surgeon a few moments' clear vision. In closing a ventricular septal defect or a defect low in the atrial septum, the atrio-ventricular bundle must be carefully avoided by accurate placement of stitches, and often a plug of "Ivalon" sponge will have to be sewn into the opening for secure closure. When the definitive procedure has been completed, the incision in the heart is sutured, the *venæ cavæ* are released, the cannulæ are removed and the wound is closed with drainage of both pleural cavities. During all this period the patient has been receiving heparin, and one of the real post-operative difficulties has been post-operative hæmorrhage. Adequate doses of "Protamine" are given, and very close observation, with exact replacement of the blood that is sucked from the chest cavities, is needed for some hours. For most congenital defects the right ventricle or the right atrium is opened. For the relief of aortic stenosis, an incision is made into the proximal part of the aorta, and this, of course, interrupts the coronary circulation. To compensate for this, Lillihei has passed a catheter through the right atrium into the

coronary sinus, and has perfused the coronary arteries in reverse. This maintains oxygenation of the myocardium and prevents suction of air into the coronary arteries from the opened aorta. The heart beats steadily and strongly through all this procedure at normal temperatures.

Conrad Lam has shown that complete cardiac arrest can be produced by the use of potassium chloride or acetylcholine, injected into the aorta just proximal to a clamp that has been placed across it so that the drug circulates in the coronary arteries. Working with hypothermia, he was impressed by the advantages of this arrest during the period of circulatory occlusion, and now that he is using a Lillihei oxygenator, he uses acetylcholine to arrest the heart during the period of by-pass. This cardiac arrest makes the surgical technique easier, and by stopping coronary flow keeps the field drier; also, of course, it lessens the chance of air embolism, even when the aorta is opened to operate on a patient with aortic stenosis.

Melrose independently developed the same idea, using potassium citrate, and this technique has been enthusiastically adopted by Kirklin. As soon as the heart has emptied itself after the *venæ cavæ* have been occluded, the aorta is clamped close to the heart and a small dose of potassium citrate, mixed with the patient's blood in a syringe, is injected into the aorta proximal to the clamp and is forced into the coronary arteries. The heart immediately stops beating and becomes flaccid. It now remains completely dry, except for a minute trickle of blood from the bronchial arteries into the left atrium. Operative technique is simplified and more precise, and even if the aorta is opened, coronary air embolism does not occur, because there is no flow in the coronary arteries.

When the incision in the heart has been closed, the clamp is removed from the aorta, blood enters the coronary arteries and washes out the potassium, and a normal heart beat is resumed. During the period of arrest, the heart is bloodless, like a limb with a tourniquet on it. It needs no oxygen, and provided the heart and aorta are filled with fluid and all air is excluded before circulation is resumed, the risk of coronary air embolism is eliminated.

Atherosclerosis of the coronary arteries, resulting in myocardial infarction, is one of the greatest killers of our age. Beck (1935) and O'Shaughnessy (1936) were the first to suggest methods for revascularization of the myocardium. Since then, many thousands of animal experiments have been carried out and many patients have been operated on, and those who have done much of this work are convinced that operations designed to develop anastomoses with the coronary vessels do work. Unfortunately, there is no objective method of assessing results, and although I would hesitate to say that the subjective improvement obtained by these patients is all psychological, I am not yet convinced of their real value.

The ultimate answer to cardiac ischæmia will come from understanding of the causes of atherosclerosis and its prevention; but, in the meantime, we may develop a technique for resecting a segment of a coronary artery and anastomosing the ends or inserting a homograft, as in many patients the fatal block is local and could be resected. For these operations a heart-lung machine with reverse coronary perfusion or potassium arrest would be required. Hypothermia at its present stage would give too little time.

To summarize, it may be said that the treatment of patent *ductus arteriosus* and coarctation is well established. Blind operation for mitral stenosis is satisfactory, but may eventually be superseded by an open technique. The closed methods for the relief of pulmonary stenosis and the repair of uncomplicated atrial septal defects have achieved a high degree of success. Hypothermia is available for those who prefer an open operation, and, of course, a machine may be used as an alternative to hypothermia. The relief of aortic stenosis by blind methods has been far from satisfactory, and it is hoped that open operation under hypothermia or on a machine may be better.

For Fallot's tetralogy, although palliative shunts have been temporarily satisfactory, the only hope of cure is in open operation on a machine, and the closure of a ventricular septal defect or a common atrio-ventricular opening is also possible only on a machine.

Mitral regurgitation has so far defied all attempts at repair; but here again the machine may be triumphant. Complete transposition of the great vessels and anomalous pulmonary venous drainage and Ebstein's anomaly are rare conditions requiring most complex cardiac plumbing for their relief; but even these are not without hope, and the time may come when excision and suture or grafting of coronary arteries may offer a new lease of life to some patients with cardiac ischæmia.

## THE L.E. PHENOMENON IN RHEUMATOID ARTHRITIS.

By the late L. J. A. PAGE, EVA A. SHIPTON, PHILIP BENJAMIN and PAUL H. H. WHITE,
*Sydney.*

### Review of the History of the Antimalarial Drugs in Disseminated Lupus Erythematosus and Rheumatoid Arthritis.

PAGE (1951) reported the effect of mepacrine in cases of *lupus erythematosus*, but was preceded by the Russian investigator Prokopchuk (1940), who stated that because of the inadequacy of the treatment of *lupus erythematosus* he had tried acriquine ("Atebrin") with excellent results. Other Russian dermatologists a little later recorded that they had also been successful in treating the disease in like manner. They did not record any particular effect on the arthritis which often accompanies *lupus erythematosus*.

It is now well known that the trial of the antimalarial drugs in rheumatoid arthritis was suggested by Page's results, as he had observed that the complicating arthritis of *lupus erythematosus* underwent remission at the same time as the rash disappeared. As a result of this observation, Freedman and Bach (1952) tried the effect of mepacrine ("Atebrin") in cases of rheumatoid arthritis without any dermatological evidence of *lupus erythematosus*, and found that in a large number the condition was favourably controlled. Some French authors also began treating patients suffering from rheumatoid arthritis with the antimalarial drugs, finding that "Atebrin" could be replaced by chloroquine just as efficaciously. The trial of chloroquine was suggested because of the objection to the staining of the skin by "Atebrin".

Since 1951 American investigators have confirmed the therapeutic effectiveness of mepacrine and chloroquine in both the discoid and disseminated forms of *lupus erythematosus*.

The report by Freedman and Bach (1952) prompted us to try the effect of mepacrine in cases of rheumatoid arthritis which we regarded as typical of that disease. Many such cases have been observed for years, and the diagnosis was not in doubt. The typical small joint involvement, the symmetrical nature of the disease, the vasospasm as shown by the cold, clammy hands and the frequent ulnar deviation gave a classical picture of rheumatoid arthritis. We had watched many of these patients for a decade and had observed the fluctuations of the arthritic storms. We also tried the effect of chloroquine, owing to the severity of the mepacrine rash which occurred in a number of cases, and also to the discoloration of the skin, to which even the responsive patients often objected. We observed remarkable improvement in many cases from the use of these drugs, and the disease in a number of cases has been controlled for years. On suspension of the drug the disease tends to recur after three to four months, a feature which can be contrasted with the rapid relapse following suspension of cortisone. These drugs have proved to be much better controlling remedies than the cortisone group of drugs in a number of cases.

Having by our own clinical experience observed the successful employment of these drugs over a period of three years, we began to search for the reason. The question arose whether all the patients who responded favourably had arthritic manifestations of disseminated *lupus erythematosus*, or were suffering from typical rheumatoid arthritis with associated L.E. cells, or whether there was a very close link between those two diseases—a fundamental basic pathology—the L.E. cell being the manifestation of common parentage. We had observed over the years the high incidence of cutaneous susceptibility of rheumatoid arthritic patients to the sulphonamide drugs when they were given over long periods in small dosage, and the frequent occurrence of photosensitivity rashes, but were also well aware of the common employment of ultra-violet light as supportive therapy in rheumatoid arthritis. It is well known that ultra-violet light is able to produce severe exacerbations of *lupus erythematosus* and can initiate a disseminated form of the disease following its application to a localized discoid form. However, a certain percentage of rheumatoid patients report that spring and summer produce an exacerbation of their disease, and we had noticed in a number of cases that the erythrocyte sedimentation rate rose during the spring and early summer and fell during the winter. Were these cases, although clinically rheumatoid, in reality arthritic manifestations of disseminated *lupus erythematosus*, which in our ignorance we had failed to recognize?

For a number of years we had recognized (clinically) two varieties of psoriasis associated with rheumatoid arthritis; in one, summer and sunlight produced exacerbation of both the rash and the arthritis; in the other, exposure to the sun or artificial light produced remission of the disease. Such an observation begs the question whether the former cases might have been associated with the L.E. cell phenomenon, whilst in the others there was no such accompanying pathological manifestation.

In 1951, Francis E. Brennecke and his co-workers treated 38 patients suffering from rheumatoid arthritis and ankylosing spondylitis with antimalarial drugs, and reported considerable improvement in 20 of the 35 cases in the rheumatoid group, whilst in the other 15 of these cases there was only minor improvement or none at all. However, the ankylosing spondylitis patients were reported as responding well to such therapy.

In 1953, Haydu also treated 28 rheumatoid arthritis patients with chloroquine; 21 showed considerable improvement. He postulated the theory that the drug depressed the activity of the enzyme adenosine triphosphatase, allowing its better utilization by the tissues. Haydu suggested that the pathology of rheumatoid arthritis was based on the high effort level of the tissues, especially for adenosine triphosphatase, and a simultaneous lack of hormonal support.

Rhinehart, in July, 1955, published his results of chloroquine therapy in rheumatoid arthritis. He advanced the theory that amœbiasis might be a factor in rheumatoid arthritis, and suggested that chloroquine acted on the *Entamœba histolytica* which he found present in the fæces of all his adult patients.

All these investigators had shown not only that the antimalarial drugs mepacrine and chloroquine had a beneficial effect in *lupus erythematosus* as well as in rheumatoid arthritis, but also that the basis of the success in rheumatoid arthritis was still shrouded in surmise and conjecture. However, ætiologically a new light has possibly dawned as a result of the recognition that hydralazine, a potent antihypertensive drug, can produce L.E. cells in the blood, as well as associated arthritis closely resembling rheumatoid arthritis. With the cessation of the drug, remission of the arthritic process and disappearance of the L.E. cells occurred.

Page, who in 1951 reported the effect of mepacrine in his 18 cases of *lupus erythematosus* and who observed the dramatic change of the accompanying rheumatoid arthritis in two cases, did not mention any effect on the L.E. cell. He remarked that the drug reduced light sensitivity, and therefore that the dermatological response could be understood, but that the relief of the joint disability was inexplicable on that basis. He observed that the beneficial response from mepacrine with regard to the skin lesion was greater than with ACTH and cortisone.

Dubois in 1955 found that quinacrine ("Atebrin") had an effect on the L.E. cell phenomenon, and that in experiments *in vitro* the drug completely inhibited the L.E. cell phenomenon at concentrations of 0·2 to 0·4 milligramme per millilitre. He noted that the highest plasma level that could be obtained in patients taking 200 milligrammes of quinacrine daily was 0·1 milligramme per 100 millilitres, but that the quinacrine concentration in the leucocytes reached 100 to 300 times the plasma level and was within the inhibitory range. He remarked that the quinacrine ("Atebrin") level in the liver, spleen and lung might be as high as 20,000 times the plasma level, and therefore that inhibition *in vivo* was easily obtainable. Dubois suggested that there were three possible modes of action of quinacrine: (i) The drug might inhibit the production of the L.E. factor in the reticulo-endothelial system, where the L.E. factor, which is a fraction of the γ-globulin, is produced. (ii) The drug might render inactive the circulating L.E. factor if prolonged exposure could be undertaken. (iii) The drug might block the intercellular action of the L.E. factor on the desoxyribonuclease system.

It would seem from the work of Dubois that an explanation of the action of "Atebrin" and chloroquine in rheumatoid arthritis might be found in their suppression of the L.E. phenomenon produced by the L.E. cell factor, if that phenomenon occurred in a percentage of cases labelled as typical rheumatoid arthritis. Dubois, however, stated that "the L.E. phenomenon is pathognomic of systemic Lupus Erythematosus in our experience and that of others". He remarked that the only exception was the rare case of hydralazine intoxication which closely resembled *lupus erythematosus*.

The arthritic manifestations of disseminated lupus generally, but not always, occur before the skin lesion. In some cases joint lesions are the outstanding feature of the disease, and in subacute and chronic cases may persist for months or even years.

Slocumb (1953) noted the occurrence of arthritis in 60% of cases of acute and subacute disseminated lupus and in 20% of the chronic cases.

In "Comroe" (Hollander *et alii*, 1953) it is stated that "the arthritis of disseminated lupus has no characteristic feature so that one must rely on the general characteristics of the disease for the diagnosis".

Hargraves *et alii* first discovered the L.E. cells in the bone marrow, and in "Comroe", in the 1953 edition, it was stated that so far the cell had been found only in cases of disseminated lupus. Further, he remarked that the arthritis was generalized and frequently resembled rheumatoid arthritis. He stated that frequently the joint symptoms were not distinguishable from those of early rheumatoid arthritis, and that the identification of the L.E. cells in the blood of the patient might prove helpful in the elucidation of the cause of the arthritic disease.

As was pointed out previously, Dubois in 1955 had also stated that the L.E. phenomenon was pathognomonic of systemic *lupus erythematosus*.

It seems obvious that many authorities would regard the presence of L.E. cells in the blood of a patient suffering from clinical rheumatoid arthritis as indicating that the disease is disseminated lupus with arthritic manifestation. The good result achieved by the antimalarial drug in rheumatoid arthritis could indicate that the physician was dealing not with true rheumatoid arthritis, but with disseminated *lupus erythematosus* with a rheumatoid-like arthritic disease.

### Trial of the Antimalarial Drugs in Rheumatoid Arthritis.

In 1952 our objective in treating patients suffering from rheumatoid arthritis with mepacrine and later chloroquine

was to see whether the disease could be controlled by these drugs and, if so, what type of patient responded. Later we have tried to find out the number of patients with rheumatoid arthritis who have L.E. cells in their blood and whether they fit into a particular pattern, or whether such cases are indistinguishable from the so-called typical rheumatoid arthritis with symmetrical small joint involvement without skin rash which occurs in systemic *lupus erythematosus*.

FIGURE I.

Case 6: The patient's elbow and forearm. This was a typical case of rheumatoid arthritis with L.E. cells. Note the nodules on the forearm.

One of the first cases which aroused our suspicion that typical rheumatoid arthritis could be associated with *lupus erythematosus* was that of a young woman who presented herself about fourteen months ago with typical vasospastic rheumatoid arthritis of hands, wrists, shoulders, knees and feet, with a history of only six weeks' duration, but without any sign of a skin rash. Her erythrocyte sedimentation rate was 117 millimetres Westergren at sixty minutes. She was given mepacrine, and in approximately two months her erythrocyte sedimentation rate had remarkably improved and was only 10 millimetres in one hour. The condition of her joints (as regards pain and swelling) had considerably improved, and the generalized pallor of her face and limbs had almost disappeared. However, at this stage a rash occurred on the forearm and the inner side of the thigh as well as on her shins, which resembled typical *lupus erythematosus*; this was confirmed later by a dermatologist. It was necessary to add cortisone to control the skin manifestation.

We then began to search for L.E. cells in new patients with rheumatoid arthritis, as well as in our older patients whom we had observed for many years.

## On Our Experiences Relating to L.E. Cells in Rheumatoid Arthritis.

We are now reporting 55 cases of rheumatoid arthritis, in 35 of which we have found L.E. cells. There are only two cases in which the dermatological appearances suggested the diagnosis of rheumatoid arthritis and *lupus erythematosus*—namely, Case 11 and Case 12. The patient in Case 11 is a female, who has had the disease for eight years and has been watched for almost two years, and we have noted the exacerbation of the disease during the summer months. She displays a typical facial rash. Her rheumatoid disease is typical of rheumatoid arthritis, and she has pronounced ulnar deviation. The radiological appearances of the hands of these patients with L.E. cells in their blood do not differ from those of patients who have not.

In 20 cases the L.E. cells were not found in the peripheral blood. These were all typical cases of rheumatoid arthritis, some of long standing, and were in no way clinically different from some of the 35 cases in which L.E. cells were found in the blood. However, only one examination was made.

We have also demonstrated L.E. cells in a number of cases of ankylosing spondylitis, lumbar fibrositis and sciatica. In one of the cases of ankylosing spondylitis, the patient, a female, had been under our supervision since late 1940, and though clinically the disease was controlled, the erythrocyte sedimentation rate remained high. In consequence, we examined the blood for L.E. cells, and they were demonstrated.

The relation of these cases to systemic *lupus erythematosus*—whether they are systemic *lupus erythematosus* or a variant of this disease, or whether L.E. cells are present in other diseases than systemic *lupus erythematosus*—has still to be elucidated.

The details are presented in Table I.

## Discussion of Cases.

### *Sex.*

There were only seven males amongst the 35 patients in whose peripheral blood the L.E. phenomenon was demonstrated, the females thus outnumbering the males by four to one. The duration of the disease varied from three months to twenty years. There were only four cases in which the rheumatic disease had been present for less than one year at the first consultation. Some of the patients have been observed for very long periods at regular intervals, up to sixteen years. Ten patients have been under observation for periods less than one year.

FIGURE II.

Case 6: The patient's hand and wrist. Note the involvement of the wrist and the metacarpal and interphalangeal joints. The radiological appearance of the hands was typical of rheumatoid arthritis.

### *Type of Disease.*

With regard to the disease, most patients had the clinical picture of rheumatoid arthritis with symmetrical small joint involvement, in some cases in only the upper limbs, but in others in both upper and lower limbs. Some had palmar erythema, skin pallor with pink finger tips, atrophic skin and typical ulnar deviation, whilst a few showed the Raynaud-like syndrome. One showed scleroderma of the hands and left leg, and one showed the *arthritis mutilans* variety. In Case 28, not only was there typical vasospasm in the hands, but also vasoconstriction was present in the face. This man was severely affected.

### *Erythrocyte Sedimentation Rate.*

The figure for the erythrocyte sedimentation rate (Westergren) is given at the end of sixty minutes, the highest being 132 millimetres in Case 25. Two of the patients had normal sedimentation rates; this shows that the L.E. phenomenon can be demonstrated even though the blood shows little sign of any active rheumatic disease.

### *Leucocyte Counts.*

The leucocyte count varied. One patient had Felty's syndrome with a leucocyte count of 2200 per cubic millimetre; in this case with cortisone therapy the disease underwent within four weeks a complete remission lasting for over three years. The highest count was 14,300 leuco-

TABLE I.

*Details of 35 Cases in which the L.E. Phenomenon was Present.*

| Case No. | Sex. | Age. (Yrs.) | Duration of Disease. | First Consultation. | Type of Disease. | Initial Erythrocyte Sedimentation Rate.[1] | Anæmia. | Leucocytes per Cubic Millimetre. | Time Under Observation. | Date when L.E. Cells Discovered, and Erythrocyte Sedimentation Rate.[1] | Rash. | Nodules. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | F. | 24 | 2½ years. | 11/12/50 | Typical bilateral symmetrical small joint involvement of hands. | 34 | Normocytic. | 13,200; neutrophile cell increase. | 6 years. | 5/11/56: 14. | – | + |
| 2 | F. | 35 | 14 years. | 28/ 9/51 | Typical bilateral symmetrical small joint involvement of hands. | 17 | Normocytic, later macrocytic. | 10,000 to 4200; normal neutrophile cell count. | 5 years, 2 months. | 3/10/56 | – | – |
| 3 | M. | 48 | 4 years. | 12/ 1/53 | Extensive rheumatoid arthritis, upper and lower limbs; palmar erythema, scleroderma. | 96 | Mild hypochromic. | 10,000; normal neutrophile cell count. | 3 years, 9 months. | 10/ 9/56 | – | + |
| 4 | F. | 36 | 18 months. | 14/ 7/50 | Extensive rheumatoid arthritis of upper and lower limbs; Raynaud-like syndrome. | 46 | Mild hypochromic. | 7000; normal neutrophile cell count. | 6 years, 4 months. | 30/10/56: 3. | – | – |
| 5 | M. | 68 | 3 years. | 31/ 8/53 | Extensive rheumatoid arthritis of upper and lower limbs; vasospastic. | 58 | Mild hypochromic. | 10,200; normal neutrophile cell count. | 3 years, 3 months. | 18/6/45: 112. | – | – |
| 6 | M. | 62 | 6 years. | 17/ 9/56 | Extensive rheumatoid arthritis of upper and lower limbs and with œdema. | 50 | — | — | 2 months. | 17/ 7/56 | – | + |
| 7 | F. | 56 | 2½ years. | 31/10/49 | Rheumatoid arthritis of upper and lower limbs; vasospastic; ulnar deviation. | 3 rose to 40 | None. | 7200 | 7 years. | 11/10/56: 1 | – | – |
| 8 | F. | 50 | 12 years. | 31/10/56 | Extensive rheumatoid arthritis of upper and lower limbs; ulnar deviation. | 17 | Mild hypochromic. | 6100 | 2 months. | 31/10/56 | – | + |
| 9 | F. | 31 | 3 years. | 24/ 7/50 | Typical rheumatoid arthritis of upper and lower limbs. | 47 | None. | 11,000; lymphocytosis. | 6 years. | 12/10/56 | – | + |
| 10 | F. | 40 | 16 months. | 15/10/56 | Periarticular rheumatoid arthritis of upper limbs. | 4 | — | — | 2 months. | 15/10/56 | – | – |
| 11 | F. | 49 | 8 years. | 8/ 2/55 | Typical rheumatoid arthritis; ulnar deviation. | 15 | Hypochromic. | 7500 | 20 months. | 1/ 8/56 | + | + |
| 12 | F. | 23 | 18 months. | 20/ 8/55 | Typical rheumatoid arthritis of upper limbs. | 10 | None. | 5200 | 15 months. | 21/ 6/56 | + | – |
| 13 | F. | 37 | 20 months. | 23/11/54 | Typical rheumatoid arthritis of upper and lower limbs; Raynaud-like syndrome. | 12 | Hypochromic. | 10,800 | 2 years. | 15/10/56 | – | – |
| 14 | F. | 26 | 5 years. | 14/12/49 | Vasospastic rheumatoid arthritis of upper and lower limbs. | 16 | None. | 9000 | 7 years. | 11/10/56 | – | + |
| 15 | F. | 32 | 2 years. | 10/ 2/50 | Generalized rheumatoid arthritis; Raynaud-like syndrome. | 18 | Hypochromic. | 6800 | 6 years, 10 months. | 11/10/56 | – | – |
| 16 | M. | 31 | 18 months. | 21/ 4/53 | Extensive rheumatoid arthritis of upper and lower limbs. | 22 | None. | 12,100; neutrophile cell increase. | 3 years, 7 months. | 4/10/56: 21 | – | – |
| 17 | M. | 44 | 2 years. | 26/ 9/56 | Extensive rheumatoid arthritis of upper and lower limbs. | 16 | — | — | 2 months. | 26/ 9/56 | – | + |
| 18 | F. | 40 | 15 months. | 7/ 8/56 | Extensive rheumatoid arthritis with scleroderma. | 18 | None. | 6700 | 3 months. | 28/ 9/56 | – | – |

[1] Millimetres in one hour.

TABLE I.—*Continued.*

*Details of 35 Cases in which the L.E. Phenomenon was Present.*—Continued.

| Case No. | Sex. | Age. (Yrs.) | Duration of Disease. | First Consultation. | Type of Disease. | Initial Erythrocyte Sedimentation Rate.[1] | Anæmia. | Leucocytes per Cubic Millimetre. | Time Under Observation. | Date when L.E. Cells Discovered, and Erythrocyte Sedimentation Rate.[1] | Rash. | Nodules. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 19 | F. | 51 | 20 years. | 19/11/40 | Typical rheumatoid arthritis of upper and lower limbs; ulnar deviation and deformity; palmar erythema. | 70 | None. | 4300 | 16 years. | 28/ 9/56 | – | + |
| 20 | M. | 39 | 12 years. | 5/ 2/51 | Typical rheumatoid arthritis of upper and lower limbs; enlarged spleen; Felty's syndrome. | 27 | Severe hypochromic. | 2200 | 5 years. | 5/10/56 | + | + |
| 21 | F. | 59 | 1 year. | 21/ 9/56 | Rheumatoid arthritis of hands and wrists. | 13 | None. | 5700 | 2 months. | 24/ 9/56 | – | – |
| 22 | F. | 35 | 6 months. | 28/ 1/55 | Early rheumatoid arthritis of upper limbs. | 5 | None. | 5700 | 1 year, 10 months. | 16/9/56: 36 | – | – |
| 23 | F. | 46 | 4 years. | 12/12/50 | Extensive rheumatoid arthritis with deformity. | 114 | Hypochromic. | 5000 | 6 years. | 28/6/56: 67 | – | + |
| 24 | F. | 72 | 3 months. | 9/10/56 | Extensive rheumatoid arthritis of upper and lower limbs. | 45 | Hypochromic. | 10,300 | 1 month. | 10/10/56: 45 | – | – |
| 25 | F. | 71 | 18 months. | 14/12/52 | Severe generalized rheumatoid arthritis of upper and lower limbs with œdema. | 77 to 125 to 132 | Hypochromic. | 12,600 | 4 years. | 27/8/56: 95 | Slight. | + |
| 26 | F. | 70 | 7 months. | 7/ 2/56 | Rheumatoid arthritis of upper and lower limbs. | 25 | None. | 7700 | 7 months. | 29/10/56 | – | – |
| 27 | F. | 66 | 6 months. | 5/ 7/50 | Rheumatoid arthritis of upper and lower limbs; Plummer-Vinson syndrome. | 65 | Marked hypochromic. | 5400 | 6 years. | 30/10/56 | – | – |
| 28 | M. | 59 | 3 months. | 30/ 9/56 | Vasospastic rheumatoid arthritis of upper and lower limbs. | 82 | Hypochromic. | 9400 | 1 month. | 11/10/56 | – | – |
| 29 | F. | 55 | 4 years. | 9/ 1/53 | Typical rheumatoid arthritis of upper and lower limbs; vasospastic; palmar erythema. | 16 | Hypochromic. | 12,000 | 3 years, 10 months. | 8/10/56: 2 | – | – |
| 30 | F. | 50 | 15 years. | 2/11/56 | Generalized severe deformity of upper and lower limbs. | 46 | Hypochromic. | 4600 | 1 month. | 3/11/56 | – | + |
| 31 | F. | 32 | 13 years. | 21/10/52 | Extensive rheumatoid arthritis of upper and lower limbs. | 23 | Hypochromic. | 8200 | 4 years. | 24/10/56: 15 | – | + |
| 32 | F. | 52 | 2 years. | 26/ 5/51 | Rheumatoid arthritis of upper and lower limbs; vasospastic. | 27 | Hypochromic. | 14,300 | 5½ years. | 19/11/56: 21 | – | – |
| 33 | F. | 34 | 1 year. | 5/ 1/50 | Vasospastic rheumatoid arthritis of hands and wrists and one knee. | 30 | Hypochromic. | Normal. | 5 years, 10 months. | 15/10/56: 6 | – | + |
| 34 | F. | 51 | 3 years. | 14/ 4/49 | Vasospastic rheumatoid arthritis of upper and lower limbs with deformity. | 54 | Slight. | 12,400 | 7½ years. | 21/9/56: 75 | – | – |
| 35 | F. | 49 | 4 years. | 22/ 7/46 | Vasospastic rheumatoid arthritis of upper and lower limbs with ulnar deviation. | 39 | Hypochromic. | 9400 | 10 years, 3 months. | 22/10/56: 47 | – | – |

[1] Millimetres in one hour.

cytes per cubic millimetre in Case 32; this was a female patient, whose extensive rheumatic disease was controlled by steroid and chloroquine therapy.

*Rash.*

A rash which resembled that of disseminated *lupus erythematosus* was seen in two cases; but there was a

suggestion of a typical rash in one other case. Therefore, on skin manifestations, only in three cases could a diagnosis be made of disseminated *lupus erythematosus* associated with clinically typical rheumatoid arthritis.

*Nodules.*

Fifteen patients of the 35 showed typical subcutaneous rheumatoid nodules in the usual parts of the upper limbs. Many of these patients, as well as some of the others, had nodules in the flexor tendons of the hands. In Case 20 extensive nodule formation was present on the dorsal surface of the fingers, associated with lymphadenopathy, splenomegaly and leucopenia.

*Wassermann and Other Tests.*

The serum of all patients failed to react to the Wassermann test. Coombs's test was not performed, nor were cold agglutinins sought. No patient had any history of abnormal hæmorrhagic manifestations.

## Conclusion.

In the 20 patients with rheumatoid arthritis in whom the L.E. phenomenon was not demonstrated, there was clinically no difference from those in whom the phenomenon was demonstrated, except when the presence of a typical rash suggested the diagnosis of disseminated *lupus erythematosus* and rheumatoid arthritis.

The blood of these patients was examined only once for the phenomenon. Only seven patients of the 35 showing the phenomenon had previously had steroid therapy.

It would seem from these observations that the L.E. cell phenomenon is much more common in rheumatoid arthritis than was previously thought. Whether the presence of the L.E. phenomenon indicates that the disease should be designated as systemic *lupus erythematosus* with arthritis rather than as rheumatoid arthritis we are not in a position at present to decide. It is possible that the phenomenon represents a particular reaction of the the connective tissues to an antigen, either bacterial or chemical—in other words, a non-specific antigen-antibody effect.

If these patients who have the L.E. phenomenon are considered to be suffering from systemic *lupus erythematosus*, the whole concept of rheumatic disease will be altered and a new approach to treatment will be necessary, with careful differentiation of the two types of disease.

Ross and Clardy (1956) found the L.E. phenomenon in 18 out of 91 patients presenting the features of a rheumatoid-like arthritis, and in these 18 there was a considerably higher incidence of multisystem involvement than in the control group. Ross and Clardy recommend that every patient presenting the rheumatoid picture should have an L.E. cell test, and that a positive result may give a warning of multisystem disease.

Goulder and Diggs (1956) state that the so-called L.E. cells are not specific for systemic *lupus erythematosus*, and report that the phenomenon was present in one case of rheumatoid arthritis.

Whether the basic pathology of rheumatoid disease, systemic *lupus erythematosus*, Sjögren's syndrome, Reiter's syndrome, Felty's syndrome, and in some cases spondylitis is similar, we still have to discover by careful clinical and laboratory tests. In every new patient complaining of rheumatism, comprehensive laboratory tests are essential both for diagnosis and for treatment.

It has been suggested by one of us (L. J. A. Parr) that the fibrinolytic system is concerned in the collagen diseases and that the mechanism which releases plasmin from plasminogin is deficient, the result being that the circulating antigens and possibly the L.E. factor are not broken down and rendered innocuous, and therefore the disease is being continually kept up.

## Summary.

A brief history of antimalarial therapy in disseminated *lupus erythematosus* has been given.

Some of the reports that prompted the use of these drugs in rheumatoid arthritis are detailed, as well as the results of such therapy.

The L.E. cell and its significance in disseminated *lupus erythematosus* are discussed, and the difficulty of ascertaining whether this cell is specific for this disease is shown.

The results of the investigation of the L.E. phenomenon in 55 cases of rheumatoid arthritis are given; the cells were found in 35 cases, whilst in 20 of which the histories are not detailed the result is stated to have been negative, although the clinical condition differed in no wise from the cases in which the cells were found. Only one examination was made in each case.

Two illustrations (Figures I and II) demonstrate the typical appearance of rheumatoid arthritis with the L.E. phenomenon in the blood.

## References.

BRENNECKER, F., ALVING, A. S., ARNOLD, J., BERGENSTAL, D. M., and DE WIND, L. T. (1951), "A Preliminary Report on the Effect of Certain 8-amino-quinolines in the Treatment of Rheumatoid Arthritis", *J. Lab. & Clin. Med.*, 38: 795.

DUBOIS, E. L. (1955*a*), "Quinacrine (Atabrine) in Treatment of Systemic and Discoid Lupus Erythematosus", *Arch. Int. Med.*, 94: 131.

DUBOIS, E. L. (1955*b*), "Effect of Quinacrine (Atabrine) upon Lupus Erythematosus Phenomenon", *Arch. Dermat.*, 71: 571.

FREEDMAN, A., and BACH, F. (1952), "Mepacrine and Rheumatoid Arthritis", *Lancet*, 2: 321.

GOULDIN, E. N., and DIGGS, L. W. (1956), "L.E. and L.E.-Like Cells: A Morphological Study", *Southern M. J.*, 49: 560.

HARGRAVES, M. M. (1954), "Systemic Lupus Erythematosus and the L.E. Cell Phenomenon", *Postgrad. Med.*, 16: 163.

HAYDU, G. G. (1953), "Rheumatoid Arthritis Therapy: A Rationale and the Use of Chloroquine Diphosphate", *Am. J. M. Sc.*, 225: 71.

HOLLANDER, J. L., ABRAMS, N. R., and others (editors) (1953), "Comroe's Arthritis and Allied Conditions", 5th Edition, Lea & Febiger, Philadelphia: 661.

PAGE, F. (1951), "Treatment of Lupus Erythematosus with Mepacrine", *Lancet*, 2: 755.

PROKOPCHUK, A. I. A. (1940), "Treatment of Lupus Erythematosus with Acriquine", *Vestn. Vener. Derm.*, Number 2-3: 23; translated by Zaker, S. J., and Gershenson, J. (1955), *Arch. Dermat.*, 71: 520.

RHINEHART, ROBERT E., (1955), "Chloroquin Therapy in Rheumatoid Arthritis", *Northwest Med.*, 54: 713.

ROSS, S. W., and CLARDY, E. K. (1956), "The L.E. Test in Patients Presenting the Clinical Picture of Rheumatoid Arthritis", *Southern M. J.*, 49: 553.

SLOCUMB, C. H. (1953), "Rheumatic Complaints during Chronic Hypercortisonism and Syndromes during Withdrawal of Cortisone in Rheumatic Patients", *Proc. Staff Meet., Mayo Clin.*, 28: 655.

# THE SIGNIFICANCE OF THE L.E. CELL TEST.

By D. C. COWLING, M.D., M.R.A.C.P., M.C.P.A.,

AND

I. D. THOMAS, M.B., B.S.,

*The Royal Melbourne Hospital, Melbourne.*

THE concept of a disseminated form of *lupus erythematosus* has been current for some years, and the disease has been linked with a number of conditions referred to collectively as collagen diseases (Klemperer, Pollak and Baehr, 1942). The observation by Hargraves *et alii* (1948) of the formation *in vitro* of *lupus erythematosus* cells (L.E. cells) in heparinized marrow has completely altered this concept. If, however, the presence of the L.E. cell phenomenon is taken as the criterion for the diagnosis of disseminated *lupus erythematosus* there is a very diverse clinical picture. This is illustrated by the results obtained with the L.E. cell test at the Royal Melbourne Hospital.

## Methods of Performing the Test.

Since the description of the original method, in which heparinized marrow preparations were used, several other

TABLE I.

*Analysis of the Presenting Diagnosis and Systems Involved.*

| Case Number. | Sex. | Age on Admission to Hospital (Years.) | Presenting Diagnosis. | Skin Disease. | Joint Involvement. | Lymphadenopathy. | Palpable Spleen. | Liver Disease. | Cardio-vascular and Pulmonary Disease. | Gastro-intestinal Disease. | Renal Disease. | Peripheral Vascular Disease. | Anæmia. | Leucopenia. | Thrombocytopenia. | Response to Cortone Test. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | F. | 25 | Disseminated *lupus erythematosus.* | Typical lupus. | Arthralgia. | – | – | — | Pleural effusion. | — | Nephrotic syndrome. | Thrombosis in femoral vein. | + | – | – | – |
| 2 | F. | 59 | Disseminated *lupus erythematosus.* | Typical lupus. | Arthralgia. | – | + | — | — | — | Albuminuria: microscopic hæmaturia. | — | – | – | – | – |
| 3 | F. | 21 | Disseminated *lupus erythematosus.* | Typical lupus. | Polyarthritis. | – | – | — | Pericarditis. | — | — | — | + | – | – | – |
| 4 | F. | 29 | Disseminated *lupus erythematosus.* | Atypical rash. | Arthralgia. | + | – | — | — | — | — | Raynaud's phenomenon. | + | – | – | + |
| 5 | F. | 39 | Disseminated *lupus erythematosus.* | Typical lupus. | Arthralgia. | + | + | — | — | Abdominal pain. | Albuminuria: pyelonephritis. | — | – | – | – | + |
| 6 | F. | — | Disseminated *lupus erythematosus.* | Atypical rash. | — | – | – | — | Severe hypertension. | — | Nephrotic syndrome. | — | + | – | – | – |
| 7 | F. | 35 | Disseminated *lupus erythematosus.* | Atypical rash. | Arthralgia. | – | – | — | Pulmonary tuberculosis: pleural effusions. | — | Pyelitis. | — | + | + | – | – |
| 8 | F. | 21 | Disseminated *lupus erythematosus.* | Atypical rash: purpura. | Polyarthritis. | – | – | — | Pneumonia. | — | Microscopic hæmaturia. | — | + | – | + | + |
| 9 | F. | 22 | Disseminated *lupus erythematosus.* | Atypical rash. | Polyarthritis. | – | – | History of jaundice. | — | — | — | — | – | – | – | – |
| 10 | F. | 40 | Rheumatoid arthritis. | Atypical rash. | Severe rheumatoid arthritis. | – | – | — | Pulmonary tuberculosis: systolic bruit in heart. | Peptic ulcer: gastrectomy. | Albuminuria: chronic nephritis. | Raynaud's phenomenon. | + | + | – | – |
| 11 | M. | 65 | Rheumatoid arthritis. | — | Severe rheumatoid arthritis. | – | – | — | — | — | — | — | + | – | – | – |
| 12 | F. | 47 | Rheumatoid arthritis. | — | Rheumatoid arthritis. | Tuberculous glands in neck. | – | — | — | — | — | — | + | – | – | – |
| 13 | M. | 50 | Rheumatoid arthritis. | — | Severe rheumatoid with suppurative arthritis. | – | – | — | Congestive cardiac failure with pericarditis. | — | Albuminuria. | — | + | – | – | + |
| 14 | M. | 34 | Rheumatoid arthritis. | — | Rheumatoid arthritis. | – | – | — | — | — | — | — | – | – | – | |
| 15 | F. | 25 | Rheumatoid arthritis. | Typical lupus. | Rheumatoid arthritis. | – | + | — | — | — | Renal biopsy—lupus changes. | — | + | – | – | + |
| 16 | F. | 33 | Rheumatoid arthritis. | Purpura. | Severe rheumatoid arthritis. | – | – | — | — | Recurring dyspepsia. | Pyelonephritis: albuminuria. | — | + | + | + | – |
| 17 | F. | 25 | Rheumatoid arthritis. | Scleroderma. | Rheumatoid arthritis. | + | + | Cirrhosis of liver. | Pleurisy: systolic bruit in heart. | Abdominal pains. | — | Severe Raynaud's phenomenon. | + | – | – | – |
| 18 | M. | 39 | Chronic hepatitis. | Scleroderma. | Arthralgia. | – | + | Chronic hepatitis (? infective). | Congestive cardiac failure. | Ulcerative colitis. | — | Raynaud's phenomenon: scleroderma. | + | – | – | + |
| 19 | F. | 21 | Chronic hepatitis. | Typical lupus. | — | – | + | Chronic infective hepatitis. | — | — | — | — | – | – | – | – |

TABLE I.—*Continued.*

*Analysis of the Presenting Diagnosis and Systems Involved.*—Continued.

TABLE II.—*Continued.*

*Analysis of the Presenting Diagnosis and Systems Involved.*—Continued.

| Case Number. | Sex. | Age on Admission to Hospital. (Years.) | Presenting Diagnosis. | Skin Disease. | Joint Involvement. | Lymph-adenopathy. | Palpable Spleen. | Liver Disease. | Cardio-vascular and Pulmonary Disease. | Gastro-intestinal Disease. | Renal Disease. | Peripheral Vascular Disease. | Anæmia. | Leucopenia. | Thrombocytopenia. | Response to Coombs Test. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 20 | F. | 75 | Subacute hepatitis. | — | — | — | — | Severe progressive hepatitis (? infective). | — | — | — | — | — | — | — | — |
| 21 | F. | 37 | Chronic hepatitis. | Atypical rash. | Arthralgia. | — | — | Chronic infective hepatitis. | — | — | Pyelitis: renal biopsy—normal. | History of thrombophlebitis. | — | — | — | — |
| 22 | F. | 15 | Chronic hepatitis. | — | — | — | + | Chronic infective hepatitis. | Pulmonary infarction and terminal bronchopneumonia. | Abdominal pains first symptom. | Recurrent pyelonephritis. | — | — | — | — | — |
| 23 | M. | 28 | Chronic hepatitis. | Secondary syphilitic rash. | Arthralgia. | — | — | Chronic alcoholic nutritional hepatitis. | Pneumonia. | Morning nausea. | — | — | — | — | — | — |
| 24 | F. | 20 | Chronic hepatitis. | — | — | — | — | Chronic infective hepatitis. | — | — | Albuminuria. | — | + | — | — | — |
| 25 | F. | 29 | Chronic hepatitis. | — | — | — | + | Chronic alcoholic nutritional hepatitis. | — | — | — | — | + | — | — | — |
| 26 | F. | 66 | Chronic hepatitis. | — | — | — | — | Chronic hepatitis; *diabetes mellitus*. | — | Carcinoma of stomach. | — | — | + | — | — | — |
| 27 | M. | 16 | Chronic hepatitis. | — | — | — | + | Chronic infective hepatitis. | — | — | — | — | — | — | — | — |
| 28 | F. | 37 | Hæmolytic anæmia. | — | Rheumatoid arthritis. | — | + | Jaundice from hæmolysis. | — | — | — | — | + | — | — | + |
| 29 | F. | 26 | Hæmolytic anæmia. | Atypical rash. | Arthralgia. | — | + | Jaundice from hæmolysis. | Severe hypertension. | Attacks of abdominal pain. | Albuminuria. | Gangrene of arm. | + | — | + | + |
| 30 | F. | — | Thrombocytopenic purpura. | — | Arthralgia. | — | + | Jaundice from hæmolysis. | Congestive cardiac failure. | — | — | — | + | + | + | + |
| 31 | F. | 56 | Thrombocytopenic purpura: myxœdema. | — | — | — | + | — | — | History of abdominal pain. | History of hæmaturia. | — | + | + | + | + |
| 32 | F. | 38 | Rheumatic carditis; mitral stenosis. | — | — | — | — | — | Mitral stenosis: pnuemonia: pleurisy. | — | — | — | — | — | — | — |
| 33 | F. | 44 | Constrictive pericarditis. | — | — | — | + | Slight jaundice. | Constrictive pericarditis: auricular fibrillation. | — | Renal biopsy—disseminated *lupus erythematosus*. | — | + | + | — | — |
| 34 | F. | 64 | Arteriosclerotic vascular disease. | — | — | — | + | — | Systolic bruit in heart. | — | — | Gangrene of fingers and toes. | + | — | + | — |
| 35 | M. | 22 | *Polyarteritis nodosa*. | Atypical rash. | Arthralgia and myalgia. | — | — | — | Asthma, pleurisy and (radiological) pulmonary infiltration. | — | — | *Polyarteritis nodosa*. | — | — | — | — |
| 36 | M. | 31 | *Polyarteritis nodosa*. | — | Arthralgia and myalgia. | — | — | — | — | — | — | *Polyarteritis nodosa* on biopsy. | — | — | — | — |
| 37 | F. | 56 | ? Buerger's disease. | — | — | — | — | — | — | Dyspepsia: rectal prolapse. | — | Eosinophilic arteritis with gangrene. | — | — | — | — |
| 38 | F. | 31 | Abdominal pains. | — | Arthralgia. | — | — | — | — | Recurrent abdominal pains. | — | Raynaud's phenomenon. | — | — | — | — |
| 39 | M. | 34 | Scleroderma. | Atypical rash: scleroderma. | Arthralgia. | — | — | — | — | Diarrhœa. | — | Raynaud's phenomenon: scleroderma. | — | — | — | — |

methods have been introduced. Variations of the two-hour clot technique (Zimmer and Hargraves, 1952) have formed the basis of many commonly used methods. Others utilize the patient's plasma or serum, and preparations of leucocytes either from peripheral blood or from marrow. These have been extended to the use of marrow from animals (Haserick, 1956). The slide method of Snapper and Nathan (1955) has the advantage that venepuncture is not required. The most recently described test is that of Zinkham and Conley (1956), in which heparinized blood is subjected to mechanical agitation in an apparatus similar to that used for erythrocyte mechanical fragility tests.

Certain procedures enhance the sensitivity of the test. The activation of the L.E. cell factor by blood coagulation is probably due to a substance derived from platelets (Lee *et alii*, 1954). The enhancing effect of mechanical agitation (Zinkham and Conley, 1956) is the result of disruption of leucocytes, which provides more accessible nuclear material. The washing of leucocytes apparently removes a normally present inhibitor to the L.E. factor (Kurnick *et alii*, 1953).

### *Choice of Methods for Routine Use.*

There is general agreement that the two-hour clot methods are sensitive; in decreasing order of sensitivity are techniques in which heparinized blood or marrow is used (Dubois, 1956). The test in which animal marrow is used is least sensitive (Haserick, 1956). The new method of Zinkham and Conley appears to be of comparable sensitivity to the two-hour clot test.

At the Royal Melbourne Hospital we have as a routine used the Magath and Winkle (1952) modification of the two-hour clot method, and more recently the technique of Zinkham and Conley in special circumstances for repeat tests. For a rough assessment of the potency of the L.E. factor we have used the serum method of Dacie (1956). This test often gives a negative result, despite a positive result in the two-hour clot test.

## Results.

The analysis of systems involved in patients giving a positive result to the two-hour clot test from 1954 to 1956 is shown in Table I. During this time we have performed approximately 400 tests, a number being repeat examinations. There have been 46 patients with positive findings. The histories of 39 of these have been reviewed; complete records of the remainder were not available. They may be divided according to their presenting symptoms, as follows.

1. Typical disseminated *lupus erythematosus*. Nine patients, all female, presented with classical disseminated *lupus erythematosus*. In some the facial rash had been quite fleeting. Nearly all developed arthralgia or polyarthritis, serous effusions and renal involvement.

2. Rheumatoid arthritis. Eight patients, including three males, presented with rheumatoid arthritis; in several cases it was crippling and of long duration, and the finding of L.E. cells was not altogether expected. Some had been treated with cortisone or ACTH, but there was insufficient evidence to suggest that the L.E. cell finding was associated with cortisone withdrawal (Slocumb, 1953).

3. Hepatitis. Ten patients presented with subacute or chronic hepatitis. In some of them this was clearly infectious; but in two patients the liver damage resulted from alcoholism with malnutrition. In certain of these patients other manifestations of disseminated *lupus erythematosus* were present, including rashes, arthralgia and renal involvement. In one the condition progressed to severe diffuse collagenosis with scleroderma and serous effusions associated with cardiac failure. There are two males in this group. Some of these cases have already been described by Joske and King (1955), and by Mackay, Taft and Cowling (1956). When the L.E. cell test was repeated by the use of the serum method of Dacie (1956) it gave negative results.

4. Hæmolytic anæmia. Four patients presented with acquired hæmolytic anæmia, and two also had severe thrombocytopenic purpura. Other manifestations suggestive of disseminated *lupus erythematosus* were usually present. The Coombs antiglobulin test produced a positive result in all cases, and the antibody present was of the cold type, trypsinized group $O_4$ cells being used.

5. Cardiac failure. In two cases the positive L.E. cell finding was rather unexpected. One patient had severe mitral stenosis and was considered to have active rheumatic disease. The other had constrictive pericarditis of unproven ætiology.

6. Peripheral vascular disease. This group includes four patients. Two had severe peripheral gangrene in both upper and lower limbs; in one the condition was considered originally to be atherosclerotic, and in the other all the findings suggested an unusual eosinophilic arteritis. In the remaining two cases the clinical picture on the patient's admission to hospital suggested a mild grade of *polyarteritis nodosa*. In other groups there were also two cases of thrombophlebitis, and there was one case of peripheral gangrene in a patient with hæmolytic anæmia.

7. Miscellaneous. One patient presented with an attack of undiagnosed abdominal pain. She also suffered from Raynaud's phenomenon, as did altogether six of the 38 patients. Another patient, a male, had scleroderma, a condition found altogether in three patients. Blood investigations were performed in most cases (see Table I). In 23 of these there was an anæmia below a hæmoglobin value of 80% (11·8 grammes per 100 millilitres), and in nine of these the result of the Coombs test was, at some stage of the disease, positive. In only six cases was there a consistent leucopenia below 4000 cells per cubic millimetre, and thrombocytopenia was present in six. In three cases eosinophilia was present. In two cases the Wassermann and Kahn reactions were positive; both patients denied a knowledge of contracting syphilis.

## Discussion.

There has been much discussion about the mechanism of the L.E. cell test. The components necessary for the test are: (i) living polymorphonuclear cells; (ii) dead cells as a source of nuclear material (with the use of Snapper's slide technique, 1955, dried cancer cells and Hodgkin's tissue are effective); (iii) a serum factor, which is a γ-globulin component. This "L.E." factor causes depolymerization of the desoxyribosenucleic acid of the nuclei of dead cells and its phagocytosis by the living polymorphonuclear cells. The experiments of Zimmermann *et alii* (1953) indicate that an anti-human leucocyte rabbit serum incubated with human leucocytes can produce cells with typical inclusion of amorphous material.

As a result of experience from the hepatitis group of patients and the finding of the L.E. cell phenomenon in cases of acquired hæmolytic anæmia, we believe that the L.E. cell test indicates the presence of auto-antibodies to a component of cell nuclei. By comparison, in the acquired hæmolytic anæmias, the presence of erythrophagocytosis has been accepted for some time as evidence of a circulating antibody to erythrocytes.

The test has been regarded as specific for disseminated *lupus erythematosus* and allied disorders (Haserick, 1956). Perhaps the positive results occurring in hypersensitivity to penicillin and other drugs are better regarded as indicating the nature of the reaction than as "false positive" results. The presence of free-lying amorphous material, the clumping of leucocytes into rosettes, and the presence of "tart" cells in any number are findings seen more commonly when the result is positive. But the presence of the typical L.E. cell, containing a large, rounded, homogeneous inclusion possessing a paler-staining tint than intact nuclear material, is the only criterion of a positive result. Surely this result is to be regarded as highly significant, although we must recognize that the clinical picture may be far removed from classical disseminated *lupus erythematosus*. In this series of patients the group with hepatitis—lupoid hepatitis (Mackay, Taft and Cowling, 1956)—is large; this is due in part to special efforts to investigate them. Because of the wide variety of clinical features, it seems better to regard the test as

specific for a group of conditions whose activity is probably due to a disorder of the self-recognition mechanism leading to production of auto-antibodies (Burnet, 1954) than necessarily to regard all patients who give a positive result to the test as having disseminated *lupus erythematosus*.


### Summary.

The histories of 39 patients giving a positive response to the L.E. cell test have been reviewed. The mechanism of the test is discussed, and it is concluded that it indicates an autoimmune phenomenon. The wide variation from the classical picture of disseminated *lupus erythematosus* is specially noted.


### References.


BURNET, F. M. (1954), "The Newer Approach to Immunity in its Bearing on Medicine and Biology", *Brit. M. J.*, 2: 189.

DACIE, J. V. (1956), "Practical Hæmatology", Churchill, London.

DUBOIS, E. L. (1956), "Systemic Lupus Erythematosus: Recent Advances in its Diagnosis and Treatment", *Ann. Int. Med.*, 44: 497.

HARGRAVES, M. M., RICHMOND, H., and MORTON, R. (1948), "Presentation of Two Bone Marrow Elements: the 'Tart' Cell and the 'L.E.' Cell", *Proc. Staff Meet., Mayo Clin.*, 23: 25.

HASERICK, J. R. (1956), "Evaluation of Three Diagnostic Procedures for Systemic Lupus Erythematosus", *Ann. Int. Med.*, 44: 497.

JOSKE, R. A., and KING, W. E. (1955), "L.E. Cell Phenomenon in Active Chronic Hepatitis", *Lancet*, 2: 477.

KLEMPERER, P., POLLACK, A. P., and BAEHR, G. (1942), "Diffuse Collagen Disease. Acute Disseminated Lupus Erythematosus and Diffuse Scleroderma", *J.A.M.A.*, 119: 331.

KURNICK, N. B., SCHWARTZ, L. I., PARISER, S., and LEE, S. L. (1953), "A Specific Inhibitor for Human Desoxyribonuclease and an Inhibitor of the Lupus Erythematosus Cell Phenomenon from Leucocytes", *J. Clin. Investigation*, 32: 193.

LEE, S. L., SCHWARTZ, L. I., and PARISER, S. (1954), "Blood Coagulation and the L.E. Cell Phenomenon", *Blood*, 9: 965.

MACKAY, I. R., TAFT, L. I., and COWLING, D. C. (1956), "Lupoid Hepatitis", *Lancet*, 2: 1323.

MAGATH, T. B., and WINKLE, V. (1952), "Technique for Demonstrating L.E. (Lupus Erythematosus) Cells in Blood", *Am. J. Clin. Path.*, 22: 586.

SLOCUMB, C. H. (1953), "Rheumatic Complaints during Chronic Hypercortisonism and Syndromes during Withdrawal of Cortisone in Rheumatic Patients", *Proc. Staff Meet., Mayo Clin.*, 28: 655.

SNAPPER, I., and NATHAN, D. J. (1955), "The Mechanics of the L.E. Cell Phenomenon Studied with a Simplified Test", *Blood*, 10: 718.

ZIMMER, F. E., and HARGRAVES, N. M. (1952), "The Effect of Blood Coagulation on L.E. Cell Formation", *Proc. Staff Meet., Mayo Clin.*, 27: 424.

ZIMMERMANN, H. J., WALSH, J. R., and HELLER, P. (1953), "Production of Nucleophagocytosis by Rabbit Antileukocytic Serum", *Blood*, 8: 651.

ZINKHAM, W. H., and CONLEY, C. L. (1956), "Some Factors Influencing the Formation of L.E. Cells. A Method for Enhancing L.E. Cell Production", *Bull. Johns Hopkins Hosp.*, 98: 102.


## INVESTIGATION OF AMINO ACIDURIA IN ERYTHROBLASTOSIS FŒTALIS AND ITS POSSIBLE RELATIONSHIP TO KERNICTERUS.


By P. J. NESTEL, M.R.A.C.P.,

*Registrar, Clinical Research Unit, Alfred Hospital,*

AND

LYDIA NESTEL, B.Sc.,

*Melbourne.*


KERNICTERUS OR CEREBRAL JAUNDICE is a post-natal condition in which certain characteristic neurological signs are associated with a deposition of bilirubin in various parts of the brain. This had led to the assumption that the bilirubin was responsible for the cerebral lesions. However, evidence is accumulating which suggests that bilirubin *per se* will stain brain tissue only after the latter has been injured by hypoglycæmia, hypoxia, irradiation *et cetera* (Day, 1947). Furthermore, Dible (1951) has pointed out that bilirubin has an affinity for necrotic tissue.

This pigmentation of the brain may then be merely fortuitous, and another toxin present in kernicterus may in fact be responsible for the underlying brain damage. Moreover, it is important to realize that neonatal conditions quite apart from hæmolytic disease, and an unduly elevated serum bilirubin level, have produced clinical signs and histological changes indistinguishable from those of kernicterus. Thus Govan and Scott have described the histological findings in the brains of infants who had died after severe anoxia. Apart from the absence of biliary staining, the lesions resembled those seen in kernicterus. Zuelzer and Mudgett (1950) described kernicterus occurring clinically in babies suffering from hæmorrhage, infections and diarrhœa.

An important aspect of the disease is the functional immaturity of the liver in the newborn. Billing *et alii* (1954) estimated that in small infants liver function was only 1% to 2% of normal, and the high incidence of kernicterus in small and premature infants is well known. Prematurity by itself, apart from hæmolytic disease, may be responsible for kernicterus.

In recent years the association of liver failure with neuro-psychiatric syndromes has been stressed. A large number of cerebral functions are interfered with, and many of the signs bear a close resemblance to those of kernicterus.

As will be discussed below, various authors have investigated the correlation between the degree of cerebral disturbance and the high blood levels of ammonia and amino acids. Ammonia and amino acids have been shown to be present in the blood, the cerebro-spinal fluid and the urine in high concentration in serious liver damage of varied ætiology (Walshe, 1953*a*). The amino aciduria may be regarded as of the "overflow" variety.

From experimental and clinical evidence, the strong possibility has arisen that these substances are responsible for the cerebral dysfunction. We have therefore investigated the degree of amino aciduria in babies with severe erythroblastosis, babies whom one could assume to be very likely to develop kernicterus.

### Methods.

The infants who were investigated fulfilled the criteria of *erythroblastosis fœtalis*. They were Rhesus-positive infants borne by Rhesus-negative mothers, and laboratory investigations revealed a positive response to the direct Coombs test and rapid hæmolysis occurring in the first twenty-four hours. All the babies required immediate exchange transfusion, and several of them required as many as three exchange transfusions whenever the serum bilirubin content exceeded 20 milligrammes per 100 millilitres.

Several babies exhibited transient twitching, mild opisthotonus and other signs of cerebral irritation; but all have survived, and at the end of six to twelve months none has yet exhibited any residual cerebral damage.

Specimens of urine were obtained daily on the first four days, each specimen representing about twelve hours' output. Chromatograms were prepared of each of the four daily specimens, and in this way it is expected that gross deviations due to differing daily urinary concentrations have been avoided.

One hundred microlitres of urine were applied to Whatman Number 1 filter paper and analysed by the method described by McKee, Nestel and Robertson (1955). The papers were developed for forty-eight hours in a 4:1 mixture of phenol and water in the first direction, and in a mixture of n-butanol, glacial acetic acid and water in the proportions of 4:1:1 respectively, for thirty-six to forty-eight hours in the second direction. The identity of individual amino acids was determined by special tests also described in the above-mentioned paper. In all eight babies were investigated. In addition, the urine of eight normal newborn babies was analysed, 100 microlitres of urine being used.

## Results.

### *Normal Babies.*

Four or five amino acids were found in each normal specimen. Altogether the following seven amino acids were found in low concentration in the urine of one or other of the infants examined: glycine, alanine, glutamine, serine, cystine, valine and taurine.

These are the usual findings in normal babies as described by other workers on much larger series.

### *Erythroblastotic Babies.*

There was little variation between the eight sets of urine examined, a similar number of amino acids being present in each, although the intensity and size of the spots representing each amino acid varied a little from set to set.

The four specimens obtained from each baby showed little variation from day to day; this indicated that the amino acid excretion was fairly constant. It should be noted that these specimens of urine were obtained at the height of the infants' jaundice and soon after exchange transfusion, but before any real improvement had taken place.

From 18 to 20 amino acids were obtained from each specimen, some in very high concentrations. A number of these amino acids are not normally detectable in the urine under the foregoing experimental conditions. The amino acids found in the highest concentration were serine, cystine, α-alanine, glutamine, taurine and glycine. Present in smaller amounts were leucine, valine, histidine, arginine, aspartic acid, proline, γ-amino butyric acid, ethanolamine, glutamic acid, hydroxy-proline, methionine sulphoxide and methyl histidine. Threonine, methionine sulphone and tryptophane were present in small amounts in some of the specimens. Thus 21 different amino acids were identified.

In addition there were two other unknown spots in close proximity to each other. These gave a yellow colour to ninhydrin, which turned brown after several hours. They did not react with isatin. Their respective Rf values were as follows: "unknown 1"—0·29 for phenol and water and 0·58 for butanol, acetic acid and water; "unknown 2"—0·27 and 0·52 respectively.

## Discussion.

Although there were no full-blown cases of kernicterus among the babies investigated, it can be reasonably assumed that this would have occurred in the majority had they not been treated. Hsia *et alii* (1952) have shown that above a bilirubin level of 20 milligrammes per 100 millilitres of serum there is a 20% incidence of kernicterus, and above 30 milligrammes per 100 millilitres there is a 50% possibility. It is also probable that exchange transfusion lowered the level of the amino acids in the plasma, and that even greater concentrations would be found in babies going on to kernicterus. As can be seen from the results, we have been able to demonstrate an amino aciduria occurring in erythroblastosis which is both quantitatively and qualitatively abnormal. That this is an "overflow" amino aciduria can be inferred from investigations carried out by Walshe (1951 and 1953*a*) into amino aciduria in liver failure.

It could be argued that this was merely an indication of liver disease and coincidental to the kernicterus. However, recently ammonia has also been found in an increased amount in erythroblastosis. This work is as yet unpublished, but is mentioned by Bessman (1956). An elevated blood ammonia level is a constant finding in incipient hepatic coma (Summerskill *et alii*, 1956).

It may be desirable, therefore, to discuss in the first place the similarity between kernicterus and the neurological manifestations of liver failure. It will then be seen that there are abnormalities in the products of nitrogen metabolism in both syndromes, and finally inferences may be drawn as to the ways in which these abnormal substances could produce the neurological disorders.

A correlation of the clinical and pathological findings in kernicterus was attempted by Evans and Polani (1950) in 16 cases of their own, together with 63 other cases collected from the literature. The diverse signs of opisthotonus, muscular twitchings and hypertonia in the neonate, and of mental retardation, chorea, athetosis and pyramidal damage in the older surviving child, corresponded to the widespread biliary staining of cerebral tissue. This staining was present in 25 out of 26 babies and affected in order of frequency the *corpora striata*, the hippocampal regions and olivary nuclei, the subthalamic nucleus of Luys, the dentate nucleus of the cerebellum, the floor of the fourth ventricle, the flocculi, the thalamus and scattered cortical areas. At a later age there was atrophy of the *globus pallidus*.

This widespread involvement is compatible with the effect of blood-borne toxins, and it is interesting to note that Fröhlich and Mirsky (1942) found an increased permeability of the hæmato-encephalic barrier in the first few days after birth. This would facilitate the damaging action of any toxin. A similarly diverse symptomatology occurs in hepatic failure. Walshe (1951) found mental changes and pyramidal signs to be most frequent, followed by choreoathetosis, Parkinsonism *et cetera*.

Such findings, together with abnormal electroencephalograms, have now been frequently reported in liver failure.

In this paper evidence has been presented that there is an increased excretion of amino acids in the urine of erythroblastotic infants, and mention has been made of the finding of an elevated blood ammonia level. For over thirty years the association of elevated blood amino acid and ammonia levels with liver failure has been under investigation.

After the demonstration by Stadie and Van Slyke in 1920 that in a case of acute liver atrophy the liver was autolysed to amino acids and peptides, Mason and Davidson (1924-1925) found a terminal rise in blood amino acid levels in animals which, after a hepatectomy, had part of their liver left in the abdomen. However, Walshe (1953*a*) holds that chromatographically the amino-acid pattern of autolysed liver differs from that found in liver failure.

It is probable that abnormal levels of amino acids and ammonia arise in one or both of two ways. Firstly, the damaged liver may fail to detoxicate or metabolize these substances as they are absorbed from the bowel, or alternately the liver may be by-passed in a portal systemic shunt. Kirk (1936) showed that there was a high level of ammonia in the portal vein.

Lately there have been many reports in which the neurological symptoms of liver failure have been aggravated by the ingestion of nitrogenous substances (Phillips *et alii*, 1952). Summerskill *et alii* (1956) found that both symptoms and blood levels of ammonia and glutamine could be influenced by the administration of ammonium chloride, dl-methionine and diets of varying protein contents. Such symptoms were relieved when the patients were also given antibiotics which inhibited the production of ammonia by bacteria in the bowel (Sherlock *et alii*, 1954). That these symptoms can be produced by a shunt alone was shown by McDermott and Adam's patient (1954), who had a surgically constructed Eck fistula.

Now that we have established the fact that amino acids and ammonia are present in excess in liver failure and are in all probability responsible for the neurological sequelæ, there still remains the elucidation of their mode of action.

Ammonia is taken up by the brain in liver failure (Bessman and Bessman, 1955). This ammonia would normally be converted by the liver into urea or would be combined with glutamic acid to form glutamine. This was the basis on which Walshe (1953*b*) recommended the use of glutamic acid, and it is interesting that he found glutamine in great excess in the cerebro-spinal fluid of his patients.

Another amino acid isolated from the cerebro-spinal fluid, and one which is normally not present, was methionine sulphoxide. This may be significant, as this

amino acid inhibits glutamic acid metabolism in *Lactobacillus arabinosus* (Waelsch *et alii*, 1946). Moreover, Krebs (1935) showed that glutamic acid was the only amino acid capable of supporting cellular respiration in the human brain. Interference with glutamic acid may therefore interfere with cellular metabolism and effective ammonia binding.

The ingestion of methionine in incipient liver failure will precipitate the patient into coma. This may be due to the formation of methyl mercaptan (Walshe and Senior, 1955), which, together with dimethyl sulphide, another derivative of methionine, is found in the urine in liver failure and is probably responsible for the characteristic *fœtor hepaticus* (Challenger and Walshe, 1954).

The toxic effect on the brain of abnormal phenylalanine metabolism is seen in phenylketonuric oligophrenia, in which reversible imbecility occurs.

Under experimental conditions, excesses of different amino acids have been injurious to the brain and other organs.

Morehead *et alii* (1945) produced tubular necrosis of kidneys with serine, and Earle and Victor (1942) found that hæmorrhagic liver necrosis followed an excess of cystine. Gullino *et alii* (1955) demonstrated toxicity of all essential amino acids, which, when injected intraperitoneally into rats, produced convulsions.

It is apparent from the foregoing discussion that the manner in which ammonia and the amino acids exert their toxicity in liver failure is still a matter for speculation.

However, a few facts stand out. At a certain stage of liver failure nitrogen metabolism becomes deranged, and certain nitrogenous substances attain a high concentration in the blood. Of these, ammonia and amino acids have been investigated most extensively in a variety of liver diseases, and we have shown that in *erythroblastosis fœtalis*, in which liver dysfunction can be quite considerable, there is a great increase in urinary amino acid excretion.

It has been shown that neonatal cerebral tissue is more strongly predisposed to structural injury by biochemical factors than is the adult brain, so that substances which in the adult produce reversible neurological disorders may leave permanent organic sequelæ in the newborn.

It is possible, therefore, that kernicterus is an irreversible lesion produced by one or several nitrogenous substances present in toxic amounts during the stage of liver insufficiency, the areas of necrosis being subsequently pigmented by bilirubin. Such an hypothesis would also be compatible with the prophylactic effect of exchange transfusion.


### Summary.

Amino acid concentrations in the urine of eight infants suffering from severe *erythroblastosis fœtalis* were investigated by the method of paper chromatography.

Amino acids were found to be present in considerably increased concentration. Altogether 21 different amino acids were identified, many of which are not found in the urine of newborn infants under normal conditions.

The influence of abnormal nitrogen metabolism on the nervous system, such as occurs in derangement of liver function, is discussed, and the hypothesis is advanced that kernicterus may have a similar ætiology.



### Acknowledgements.

I wish to thank Dr. J. M. M. Drew, Superintendent of Royal Hobart Hospital, for the hospital facilities, and Dr. A. Hewson and Dr. G. Dixon, obstetrical registrars, for their cooperation.


### References.


BESSMAN, S. P. (1956), Editorial, *Ann. Int. Med.*, 44: 1037.

BESSMAN, S. P., and BESSMAN, A. N. (1955), "The Cerebral and Peripheral Uptake of Ammonia in Liver Disease with an Hypothesis for the Mechanism of Hepatic Coma", *J. Clin. Investigation*, 34: 622.

BILLING, B. H., COLE, P. G., and LATHE, G. H. (1954), "Increased Plasma Bilirubin in Newborn Infants in Relation to Birth Weight", *Brit. M. J.*, 2: 1263.

CHALLENGER, F., and WALSHE, J. M. (1954), "Methyl Mercaptan in Relation to Fœtor Hepaticus", *Biochem. J.*, 58: 28.

DAY, R. (1947), "Kernicterus Problem: Experimental In Vivo and In Vitro Staining of Brain Tissue with Bilirubin", *Am. J. Dis. Child.*, 73: 241.

DIBLE, J. H. (1951), "Degeneration Necrosis and Fibrosis in Liver", *Brit. M. J.*, 1: 833.

EARLE, D. P., and VICTOR, J. (1942), "Effect of Various Diets on Liver Damage Caused by Excess Cystine", *J. Exper. Med.*, 75: 179.

EVANS, P. R., and POLANI, P. E. (1950), "The Neurological Sequelæ of Rh Sensitisation", *Quart. J. Med.*, 19: 129.

FRÖHLICH, A., and MIRSKY, I. A. (1942), "Susceptibility to Convulsions in Relation to Age; Influence of Bile in Rats", *Proc. Soc. Exper. Biol. & Med.*, 50: 25.

GOVAN, A., and SCOTT, J. (1953), "Kernicterus and Prematurity", *Lancet*, 1: 611.

GULLINO, P., WINITZ, M., BIRNBAUM, S., CORNFIELD, J., OTEY, M., and GREENSTEIN, J. (1955), "The Toxicity of Individual Amino Acids in Rats", *Arch. Biochem. & Biophys.*, 58: 253.

HSIA, D. Y., GELLIS, S. S., and DIAMOND, L. K. (1952), "Erythroblastosis Fœtalis: Studies of Serum Bilirubin in Relation to Kernicterus", *New England J. Med.*, 247: 668.

KIRK, E. (1936), "Amino Acid and Ammonia Metabolism in Liver Disease", *Acta med. scandinav.*, Supplement 77: 1.

KREBS, H. A. (1935), "Metabolism of Amino Acids; Deamination of Amino Acids", *Biochem. J.*, 29: 1620.

MASON, E. C., and DAVIDSON, C. S. (1925), "Study of Tissue Autolysis in Vivo", *J. Lab. & Clin. Med.*, 10: 622.

McDERMOTT, W., and ADAMS, R. D. (1954), "Episodic Stupor Associated with Eck Fistula in Human with Particular Reference to Ammonia Metabolism", *J. Clin. Investigation*, 33: 1.

McKEE, H. S., NESTEL, L., and ROBERTSON, R. N. (1955), "Physiology of Pea Fruits; Soluble Nitrogen Constituents", *Australian J. Exper. Biol. & Med. Sc.*, 8: 467.

MOREHEAD, R. P., FISHERMAN, W. H., and ARTOM, C. (1945), "Renal Injury in Rat Following Administration of Serine", *Am. J. Path.*, 21: 803.

PHILLIPS, G. B., SCHWARTZ, R., GABUZDIE, G., and DAVIDSON, C. S. (1952), "Syndrome of Impending Hepatic Coma in Patients with Cirrhosis of Liver Given Certain Nitrogenous Substances", *New England J. Med.*, 247: 239.

SHERLOCK, S., SUMMERSKILL, W. H. J., WHITE, L. P., and PHEAR, E. A. (1954), "Portal Systemic Encephalopathy: Neurological Complications of Liver Disease", *Lancet*, 2: 453.

STADIE, N. C., and VAN SLYKE, D. D. (1920), "The Effect of Yellow Atrophy on Metabolism and Composition of the Liver", *Arch. Int. Med.*, 25: 692.

SUMMERSKILL, W. H. J., DAVIDSON, E. A., SHERLOCK, S., and STEINER, R. E. (1956), "The Neuropsychiatric Syndrome Associated with Hepatic Cirrhosis and an Extensive Collateral Circulation", *Quart. J. Med.*, 25: 245.

WAELSCH, H., OWADES, P., MILLER, H. K., and BOREK, E. (1946), "Glutamic Acid Antimetabolites: The Sulphoxide Derived from Methionine", *J. Biol. Chem.*, 166: 273.

WALSHE, J. M. (1951), "Observations on the Symptomatology and Pathogenesis of Hepatic Coma", *Quart. J. Med.*, 20: 421.

WALSHE, J. M. (1953*a*), "Disturbances of Ammonia Metabolism Following Liver Injury", *Quart. J. Med.*, 22: 483.

WALSHE, J. M. (1953*b*), "The Effect of Glutamic Acid on the Coma of Hepatic Failure", *Lancet*, 1: 1075.

WALSHE, J. M., and SENIOR, B. (1955), "Disturbance of Cystine Metabolism in Liver Disease", *J. Clin. Investigation*, 34: 302.

ZUHLZER, W. W., and MUDGETT, R. T. (1950), "Kernicterus: Ætiologic Study Based on Analysis of 55 Cases", *Pediatrics*, 6: 452.


## Reports of Cases.

### A CONTRIBUTION TO THE STUDY OF COLLAGEN DISEASE AND THE L.E. PHENOMENON.


By EVA A. SHIPTON,

*Sydney.*


THE recent advances in the study of collagen disease and the knowledge of the protean manifestations of systemic *lupus erythematosus* have altered our approach to diagnosis in many cases, especially chronic illness.

Hargreaves (1954) has stated that systemic *lupus erythematosus* is usurping the place of syphilis as the great impersonator.

A small series of cases is reported here, in all of which the L.E. phenomenon was demonstrated by the clotted peripheral blood test. For descriptive purposes the cases are described under the clinical diagnosis as follows: (i) Sjögren's syndrome and Plummer-Vinson syndrome; (ii) liver disease; (iii) pernicious anæmia; (iv) alopecia; (v) Raynaud's disease; (vi) arthritis.

### Sjögren's Syndrome and Plummer-Vinson Syndrome.

#### *Case I.*

This case was reported in 1949, the year in which the diagnosis was made. Since then the condition of the patient (Mrs. L.) has remained more or less stationary. During the last two winters she has suffered from several attacks of pneumonia. Arthritis has not developed, but various muscular aches and pains are present. The intense dryness of the mouth, eyes and skin remains, and severe dysphagia has recently developed. Recurrent parotitis is troublesome and lymphadenopathy is present. The L.E. phenomenon was demonstrated in the peripheral blood. Other laboratory tests gave the following results. The serum failed to react to the Wassermann test, and the Coombs test produced a negative result. The sedimentation rate was 37 millimetres at the end of one hour. The blood count was normal and the hæmoglobin value was 13·3 grammes *per centum*. The total serum protein content was 8·8 grammes *per centum*. The result of examination of the serum proteins by electrophoresis was as follows:

| | | |
|---|---|---|
| Albumin | 3·8 | grammes *per centum* |
| $\alpha_1$ Globulin | 0·05 | gramme *per centum* |
| $\alpha_2$ Globulin | 0·7 | gramme *per centum* |
| $\beta$ Globulin | 1·1 | grammes *per centum* |
| $\gamma$ Globulin | 3·1 | grammes *per centum* |

#### *Case II.*

The condition of Miss F. was diagnosed five years ago as Sjögren's syndrome, because of parotitis, arthritis, and dryness of the eyes and mouth. The patient's condition gradually became worse, and she developed many other symptoms; the diagnosis was altered to systemic *lupus erythematosus*. At present the erythrocyte sedimentation rate was 79 millimetres at the end of one hour. The total serum protein content was 8·8 grammes *per centum*. The result of examination of the serum proteins by electrophoresis was as follows:

| | | |
|---|---|---|
| Albumin | 4·4 | grammes *per centum* |
| $\alpha_1$ Globulin | 0·3 | gramme *per centum* |
| $\alpha_2$ Globulin | 0·6 | gramme *per centum* |
| $\beta$ Globulin | 1·1 | grammes *per centum* |
| $\gamma$ Globulin | 2·4 | grammes *per centum* |

The L.E. phenomenon was very pronounced. A few atypical lymphocytes were seen in the blood films. The serum failed to react to the Wassermann test, and Coombs's test produced a negative result.

#### *Case III.*

Mrs. D. had *arthritis mutilans*, with the typical dry eyes and mouth of Sjögren's syndrome and a history of parotitis. The L.E. phenomenon was present. The erythrocyte sedimentation rate was 46 millimetres at the end of one hour. A blood count gave the following information: in the red cells there were a few small forms and a few polychromatic forms; the white cells were normal; the hæmoglobin value was 12·3 grammes *per centum*.

#### *Comment.*

Morgan (1954) has stressed the systemic nature of Mikulicz's disease and its relation to Sjögren's syndrome. One of Morgan's patients with Mikulicz's disease died of systemic *lupus erythematosus*.

Morgan and Raven (1952) have published a detailed discussion of the pathology of the parotid glands in Sjögren's syndrome, and stress that the changes are specific.

Ramage and Kinnear (1956) describe six cases of Sjögren's syndrome. In two, rheumatoid arthritis was present; of the remaining four cases, there was one of polyarteritis nodosa, one of disseminated *lupus erythematosus*, one of Boeck's sarcoidosis and one of acroscleroderma.

As polyarthritis and muscle manifestations occur in sarcoid (Myers, 1952), a new approach to the study of this disease from the angle of collagen disease would be advisable.

Parotitis, common in Sjögren's syndrome, has been observed in systemic *lupus erythematosus* (Shearn and Pirofsky, 1952), and enlargement of the lymph nodes is frequent in systemic *lupus erythematosus* (Fox and Rosahn, 1943; Milnes, 1953), in rheumatoid arthritis (Motulsky *et alii*, 1952), in Sjögren's syndrome, in Felty's syndrome, and in sarcoid.

Mortenson and Gormsen (1952) believe that in systemic *lupus erythematosus* the histological changes in the lymph nodes may be suggestive of the correct diagnosis. Several cases of Sjögren's syndrome have been reported in which scleroderma was an accompanying feature (Sheldon, 1939; Harrington and Dewar, 1951), and the relation of scleroderma to systemic *lupus erythematosus* and dermatomyositis is still under discussion (Talbott, 1956). Raynaud's syndrome, commonly seen in the collagen diseases, is seen in Sjögren's syndrome (Bruce, 1941).

No instance of hæmolytic anæmia in Sjögren's syndrome is on record; but normocytic anæmia is common and macrocytic anæmia has been reported. In Cases I and II reported here, the response to the Coombs test was negative. In Case II some atypical lymphocytes were present. These lymphocytes were seen in four cases of systemic *lupus erythematosus* reported by Michael *et alii* (1951).

Arthritis is such a frequent finding in Sjögren's syndrome as to be regarded as part of it, and Gurling (1953) has reported two cases in which features of both Sjögren's syndrome and Felty's syndrome were combined.

Dysphagia is a symptom common to systemic *lupus erythematosus*, scleroderma, Sjögren's syndrome and the Plummer-Vinson syndrome. Michelson (1956) has frequently seen it in systemic *lupus erythematosus*, and thinks it is central in origin.

Godfredson (1947) believed that Sjögren's syndrome differed essentially from Plummer-Vinson syndrome and ariboflavinosis, in spite of numerous common clinical features; but recently two cases of Plummer-Vinson syndrome have been observed in which the L.E. phenomenon was demonstrable in the peripheral blood.

#### *Case IV.*

Mrs. G., aged seventy years, had complained of arthritis and difficulty in swallowing at the age of sixty-six years. She then had hypochromic anæmia and complete achlorhydria. Both the arthritis and the difficulty in swallowing solid food decreased, until at present the arthritis has almost disappeared, but some difficulty with swallowing still persists and her tongue is very sore. The L.E. phenomenon was demonstrated in the peripheral blood. The erythrocyte sedimentation rate was 14 millimetres at the end of one hour (Westergren). The hæmoglobin value was 12·4 grammes *per centum*.

#### *Case V.*

Mrs. D. presented with severe hypochromic microcytic anæmia and a history of being unable to swallow solid foods for some years. She was very emaciated and ill. With iron therapy and attention to diet she improved. When her hæmoglobin value had risen to 11·8 grammes *per centum* the erythrocyte sedimentation rate was found to be 35 millimetres at the end of one hour (Westergren). L.E. cells were demonstrated in the peripheral blood; they were scanty, but obvious. On being closely questioned, the patient admitted that she had not been really well for years, and was unable to recall when she had eaten solid food easily.

#### *Comment.*

Cardell and Gurling (1954) conclude that, although Sjögren's syndrome must be placed for the present in the ill-defined group of collagen diseases, it is pathologically

and clinically a distinct entity. The demonstration of the L.E. phenomenon by Maclean and Robinson (1954), and the finding of the L.E. phenomenon in the cases reported here suggest that not only Sjögren's syndrome, but in some cases of the Plummer-Vinson syndrome, will in future be grouped with the collagen diseases.

### Liver Disease.

*Case VI.*

Miss E., aged twenty-two years, has been under observation with liver function tests since 1952. She had a history of viral hepatitis; but the onset was unusual, since before jaundice was clinically apparent œdema of the legs was noted. Examination of the blood on October 19, 1956, gave the following results: the zinc sulphate turbidity was 29 units (normal, 0 to 12 units) and the thymol turbidity was 14 units (normal, 0 to 12 units); the serum bilirubin content was 3·0 milligrammes per 100 millilitres; the serum alkaline phosphatase content was 5·5 units. The response to the Wassermann test was negative. The L.E. phenomenon was demonstrated. The total serum protein content was 7·3 grammes *per centum*, and electrophoresis gave the following findings:

| | |
|---|---|
| Albumin | 3·6 grammes *per centum* |
| $\alpha_1$ Globulin | 0·2 gramme *per centum* |
| $\alpha_2$ Globulin | 0·5 gramme *per centum* |
| $\beta$ Globulin | 0·6 gramme *per centum* |
| $\gamma$ Globulin | 2·4 grammes *per centum* |

*Comment.*

The question as to whether this patient has chronic viral hepatitis or jaundice and liver disease secondary to systemic *lupus erythematosus* is an open one. It may be solved in the future. Bearn, Kunkel and Slater (1956), in a discussion of chronic liver disease in young women, found L.E. cells in one patient.

Joske and King (1955) demonstrated L.E. cells in a patient with active chronic viral hepatitis who developed the L.E. syndrome, and in one other who had active chronic viral hepatitis, but no clinical manifestation of systemic *lupus erythematosus*. These investigators believe that the L.E. cell phenomenon, while characteristically occurring in systemic *lupus erythematosus*, has a more general significance in indicating the presence of auto-antibodies to leucocytes.

Heller *et alii* (1956) found the L.E. cell phenomenon in two cases of post-necrotic cirrhosis, in neither of which could other signs of systemic *lupus erythematosus* be demonstrated. They regard their results as a biological false-positive result to an L.E. test, occurring in hepatic disease. Jaundice occurred in four of the cases reported by Shearn and Pirofsky (1952); in one hepatitis was suspected, and in another advanced miliary tuberculosis was present with hepatic involvement. In both of Haserick's (1955) two cases of hepatitis jaundice was associated with a worsening of the condition.

Dubois (1953) presents an illustration of an arteritis lesion in the liver of a girl, aged nine years, with classical systemic *lupus erythematosus*, and Kofman (1955) made microscopic studies of the liver from 11 patients—five biopsies and six autopsy specimens. No consistent histological abnormality was noted. Small, scattered granulomata were seen in the liver tissue of one patient, and in one centrilobular necrosis was present.

Mortensen and Gormsen (1952), in eight cases examined *post mortem*, found fatty degeneration in all, and granulomata of the intima in the central veins in one, while in one case reported by Griffith and Vural (1951) there was some necrosis of the liver cells.

Further work is needed concerning this question of the L.E. phenomenon in liver disease, and liver biopsies in proven cases of systemic *lupus erythematosus* would be of help. Another questionable point is whether some patients with liver disease and hæmolytic anæmia are suffering from systemic *lupus erythematosus* and not viral hepatitis.

### Pernicious Anæmia.

*Case VII.*

Mrs. L., aged eighty-four years, had suffered from pernicious anæmia since 1930, but has responded to adequate therapy. Two years ago she complained of not being well, and entered hospital for radiological and other investigations. The radiological examination revealed no abnormality. At that time the blood count was normal, but the erythrocyte sedimentation rate was 105 millimetres at the end of one hour (Westergren). The total serum protein content was 6·4 grammes *per centum* (albumin 3·9 grammes, globulin 2·5 grammes *per centum*). Since then her health has been causing concern. On October 11, 1956, the number of erythrocytes had fallen to 2,000,000 per cubic millimetre and the hæmoglobin value to 6·3 grammes *per centum*, and the L.E. phenomenon was demonstrated in the blood. The total serum protein content was 6·2 grammes *per centum*, and the electrophoretic pattern was as follows:

| | |
|---|---|
| Albumin | 2·7 grammes *per centum* |
| $\alpha_1$ Globulin | 0·5 gramme *per centum* |
| $\alpha_2$ Globulin | 0·4 gramme *per centum* |
| $\beta$ Globulin | 0·7 gramme *per centum* |
| $\gamma$ Globulin | 1·9 grammes *per centum* |

This patient was examined again three weeks later. At that stage the erythrocytes numbered 4,030,000 per cubic millimetre and the hæmoglobin value was 9·1 grammes *per centum*. Many macrocytes were seen in the erythrocytes, and the sedimentation rate was 130 millimetres at the end of one hour (Westergren). The direct Coombs test produced a positive result at 1:16. The total serum protein content was 5·5 grammes *per centum*, and the electrophoretic pattern was as follows:

| | |
|---|---|
| Albumin | 4·1 grammes *per centum* |
| $\alpha_1$ Globulin | 0·7 gramme *per centum* |
| $\alpha_2$ Globulin | 0·2 gramme *per centum* |
| $\beta$ Globulin | 0·1 gramme *per centum* |
| $\gamma$ Globulin | 0·4 gramme *per centum* |

*Comment.*

There is one other example on record of L.E. cells in a case of pernicious anæmia in relapse (Berman *et alii*, 1950).

The significance of the finding of L.E. cells in the present case is questionable; but the clinical history and the results of the pathological examination are in keeping with the diagnosis of systemic *lupus erythematosus* complicating pernicious anæmia. In one other case of long-standing pernicious anæmia the patient has been examined for L.E. cells with negative result. Further patients will be examined as the opportunity arises. It is interesting to speculate whether the pigment derangement in this disease could cause harm to the liver cells, with consequent formation of antigen.

### Alopecia.

*Case VIII.*

Mrs. B., aged sixty years, had not been well for eighteen months; she complained of intense fatigue. Six months earlier her hair had started to fall out so badly that hardly any hair was left on her head. About this time she had a "bad leg", the description of which suggests a thrombosis, and then a severe staphylococcal infection of one buttock, which was cured by antibiotics. There is a vague, long-standing history of "anæmia" treated with injections of liver and iron from time to time.

When the patient was examined the blood count was normal. The erythrocyte sedimentation rate was 10 millimetres at the end of one hour (Westergren), and the L.E. phenomenon was demonstrated in her blood.

*Comment.*

Disturbances of the growth of hair are not uncommon in the collagen diseases.

Alopecia occurred in 13 of the 34 cases discussed by Shearn and Pirofsky (1952), and Epstein's patient (1954) lost most of her scalp hair, which later grew again.

Evans (1953) reported alopecia in acute systemic *lupus erythematosus*, scleroderma and dermatomyositis, and Parkes Weber (1947) saw it in a case of Sjögren's syndrome.

Hypertrichosis is occasionally seen in rheumatic fever and Still's disease. Lichtwitz (1944) and Reich and Reinhart (1948) have reported it in dermatomyositis.

Hair growth appears to be influenced by changes in the connective tissue (Asboe-Hansen, 1954).

### Raynaud's Phenomenon.

*Case IX.*

Mrs. F., aged sixty-eight years, had arrived the previous week from England. She had not been well for thirty years, and had been treated by various doctors and told she was neurotic. No organic disease had been found. She had always felt the cold, and at times her fingers and toes would be "blue".

When she was examined her hands were affected. The L.E. phenomenon was demonstrated in the peripheral blood. Cold agglutinins were not detected. The erythrocyte sedimentation rate was six millimetres at the end of one hour. The blood count was normal. The hæmoglobin value was 12·6 grammes *per centum*. The total serum protein content was 6·4 grammes *per centum*; the electrophoretic pattern was as follows:

| | |
|---|---|
| Albumin | 4·8 grammes *per centum* |
| $\alpha_1$ Globulin | 0·2 gramme *per centum* |
| $\alpha_2$ Globulin | 0·5 gramme *per centum* |
| $\beta$ Globulin | 0·5 gramme *per centum* |
| $\gamma$ Globulin | 0·4 gramme *per centum* |

*Comment.*

This case is an illustration of the mild, chronic type of systemic *lupus erythematosus*. Raynaud's syndrome may develop in systemic *lupus erythematosus*, in scleroderma, in Sjögren's syndrome or in dermatomyositis, either early in the disease or later, when the condition is established.

As cold agglutinins or cryoglobulins in the serum are a cause of Raynaud's disease, and as both may occur in systemic *lupus erythematosus*, the finding of either should lead to a search for L.E. cells in all cases of Raynaud's disease.

In the case here reported no previous laboratory tests had been performed.

### Arthritis.

The question of arthritis and its relation to systemic *lupus erythematosus* is an important and controversial one. Only three cases in which the L.E. phenomenon was present are mentioned here; they emphasize the wide differences that exist in the rheumatic manifestation of systemic *lupus erythrematosus*.

*Case X.*

Miss C., aged twenty-eight years, was diagnosed as suffering from rheumatoid arthritis three years ago. The erythrocyte sedimentation rate was 115 millimetres at the end of one hour (Westergren). Her condition improved with salicylate therapy and the sedimentation rate dropped to 20 millimetres in one hour. After a few months she relapsed, with a sedimentation rate of 70 millimetres in one hour. This remained high, and L.E. cells were then found in her blood in large numbers.

*Case XI.*

Mr. C., aged twenty-three years, had been treated for rheumatic fever in the country, but was supposed to have reacted to salicylates with a purpuric rash. The pain continued in joints and muscles, but otherwise the patient felt fairly well, although fatigue was a source of complaint. The erythrocyte sedimentation rate was normal. The blood count was normal, but L.E. cells were demonstrated in the blood.

*Case XII.*

Mrs. H., aged sixty-six years, complained of arthritis in her wrist, present for six weeks. She had been well until four years ago, when she had a nervous breakdown. The erythrocyte sedimentation rate was 15 millimetres at the end of one hour (Westergren). The blood count was normal. The L.E. phenomenon was demonstrated in the blood.

*Comment.*

These patients were sent for various laboratory examinations, and either the predominant symptom or sign or the outstanding points of their histories led to the search for L.E. cells. It has been known for many years that arthritis is a prominent symptom in systemic *lupus erythematosus*.

Haserick (1955) stressed that common components of the lupus diathesis were a history suggestive of rheumatic fever, rheumatoid arthritis or glomerulonephritis, and raises the question: "Is L.E. really malignant rheumatoid arthritis or is rheumatoid arthritis benign L.E.?"

In the group of patients studied by Brunsting *et alii* (1956), 95% presented symptoms of arthralgia or arthritis, while 14% showed Raynaud's phenomenon on exposure to cold.

Freidman *et alii* (1953) used the term "pararheumatic" for rheumatism and arthritis occurring in systemic *lupus erythematosus*, *polyarteritis nodosa*, diffuse scleroderma and dermatomyositis. They describe three types: (i) myalgias and arthralgias; (ii) acute and subacute migratory polyarthritis; (iii) chronic progressive deforming polyarthritis. They also stress the fact that systemic *lupus erythematosus* or the related diseases should be suspected in the following conditions: (i) fibrositis associated with fever; (ii) acute or subacute polyarthritis with a downward course; (iii) fulminating deforming polyarthritis; (iv) atypical rheumatoid arthritis; (v) arthritis with bizarre cutaneous lesions.

If these suggestions are borne in mind and L.E. cells are sought for and other relevant laboratory tests are carried out, the diagnostic label of many arthritics will be altered.

### Discussion.

With our modern knowledge of systemic *lupus erythematosus* it appears that the blood of any patient with chronic disease should be investigated for the L.E. phenomenon.

In all the cases discussed here the serum failed to react to the Wassermann test. However, a point that needs stressing is the fact that biological "false positive" results to tests for syphilis are common in systemic *lupus erythematosus*.

Moore and Mohr (1952) were the first to give reasons for believing that the biological "false positive" reaction for syphilis is not to be dismissed lightly, but is often a manifestation of serious underlying disease, and that the collagen diseases, in which systemic *lupus erythematosus*, *polyarteritis nodosa*, rheumatoid arthritis, rheumatic fever and sarcoid are included, form a substantial proportion of such diseases.

Haserick and Long (1952) stress that the biological "false positive" result to tests for syphilis may precede by months or years other symptoms of systemic *lupus erythematosus*. Moore and Lutz (1955) suggest that the course of systemic *lupus erythematosus* may differ in subjects with chronic diseases who give biological "false positive" reactions from that in the patients with systemic *lupus erythematosus* whose serum does not react to the Wassermann test.

In view of these statements, if the serum of a patient with chronic disease gives a positive reaction to the Wassermann test, it is advisable to examine the blood for L.E. cells. This should also be done if an unexpected positive reaction is found during the routine tests in pregnancy.

**The findings of Clark and Bailey (1956) indicate that the examination of the blood for the L.E. phenomenon may play an important part in the assessment of the psychiatric patient.**

**Further work, with exact correlation of clinical and laboratory findings, is essential to gauge the importance of the L.E. phenomenon, and it is only by the continual search for L.E. cells in connective tissue disorders with their associated protean clinical manifestations that some of this knowledge will be obtained.**


### Summary.

**A small series of cases with various clinical diagnoses, in which the L.E. phenomenon was demonstrated in the blood, is reported.**


### References.


ASBOE-HANSEN, G. (1954), "Connective Tissue in Health and Disease", Munksgaard, Copenhagen.

BEARN, A. G., KUNKEL, H. G., and SLATER, R. J. (1956), "The Problem of Chronic Liver Disease in Young Women", *Am. J. Med.*, 21: 3.

BERMAN, L., AXELROS, A. R., GOODMAN, H. L., and MCCLAUGHRY, R. L. (1950), "So-Called 'Lupus Erythematosus Inclusion Phenomenon' of Bone Marrow and Blood", *Am. J. Clin. Path.*, 20: 403.

BRUCE, G. M. (1941), "Keratoconjunctivitis Sicca", *Arch. Ophth.*, 26: 945.

BRUNSTING, L. A., STICKNER, J. M., PEASE, G. L., and REED, W. B. (1956), "The Clinical Significance of the L.E. Clot Test", *Arch. Dermat.*, 73: 307.

CARDELL, B. S., and GURLING, K. J. (1954), "Observations on the Pathology of Sjögren's Syndrome", *J. Path. & Bact.*, 68: 137.

CLARK, E. C., and BAILEY, A. A. (1956), "Neurological and Psychiatric Signs Associated with Systemic Lupus Erythematosus", *J.A.M.A.*, 160,: 455.

DUBOIS, E. L. (1953), "The Effect of the L.E. Cell Test on the Clinical Picture of Systemic Lupus Erythematosus", *Ann. Int. Med.*, 38: 1265.

EPSTEIN, E. (1954), "Acute Disseminated Lupus Erythematosus", *Arch. Dermat.*, 69: 641.

EVANS, C. D. (1953), "An Unusual Alopecia Capitis in Acute Systemic Lupus Erythematosus, Scleroderma and Dermatomyositis", *Brit. J. Dermat.*, 65: 212.

FOX, R. A., and ROSAHN, P. D. (1943), "The Lymph Nodes in Disseminated Lupus Erythematosus", *Am. J. Path.*, 19: 73.

FREIDMAN, H. H., SWARTZ, S., TRUBEK, M., and STEINBROCKER, O. (1953), "The Para Rheumatic Arthropathies", *Ann. Int. Med.*, 38: 732.

GODFREDSON, E. (1947), "Relation between Sjögren's Disease, the Plummer-Vinson Syndrome and Ariboflavinosis", *Acta ophth.*, 25: 95.

GRIFFITH, G. C., and VURAL, I. L. (1951), "Acute and Sub-Acute Disseminated Lupus Erythematosus: A Correlation of Clinical and Post-Mortem Findings in 18 Cases", *Circulation*, 3: 492.

GURLING, K. J. (1953), "Association of Sjögren's and Felty's Syndromes", *Ann. Rheumat. Dis.*, 12: 212.

HARGREAVES, M. M. (1954), "Systemic Lupus Erythematosus and the L.E. Phenomenon", *Post Graduate Med.*, 16: 164.

HARRINGTON, A. B., and DEWAR, H. A. (1951), "A Case of Sjögren's Syndrome with Scleroderma", *Brit. M. J.*, 1: 1302.

HASERICK, J. R. (1955), "Modern Concepts of Systemic Lupus Erythematosus. A Review of 126 Cases", *J. Chron. Dis.*, 1: 317.

HASERICK, J. R., and LONG, R. (1952), "Systemic Lupus Erythematosus: Preceded by False Positive Serologic Tests for Syphilis: Presentation of Five Cases", *Ann. Int. Med.*, 37: 559.

HELLER, P., ZIMMERMANN, H. J., and ROZENGVAIG, S., and SINGER, K. (1956), "The L.E. Cell Phenomenon in Chronic Hepatic Disease", *New England J. M.*, 254: 1161.

JOSKE, R. A., and KING, W. E. (1955), "The L.E. Cell Phenomenon in Active Chronic Viral Hepatitis", *Lancet*, 2: 477.

KOFMAN, S., JOHNSON, G. C., and ZIMMERMANN, H. J. (1955), "Apparent Hepatic Dysfunction in Lupus Erythematosus", *Arch. Int. Med.*, 95: 669.

LITHTWITZ, L. (1944), "Pathology and Therapy of Rheumatic Fever", Grune & Stratton, New York: 123.

MACLEAN, K., and ROBINSON, H. S. (1954), "Sjögren's Syndrome", *Canadian M. A. J.*, 71: 597.

MICHAEL, S. R., VURAL, I. L., BASSEN, F. A., and SCHAEFER, L. (1951), "The Hæmatologic Aspects of Disseminated (Systemic) Lupus Erythematosus", *Blood*, 6: 1059.

MICHELSON, H. (1956), *Arch. Dermat.*, 73: 411.

MOORE, J. F., and LUTZ, W. R. (1955), "The Natural History of S.L.E.: An Approach to its Study through Chronic Biologic False Positive Reactors", *J. Chron. Dis.*, 1: 297.

MOORE, J. F., and MOHR, C. F. (1952), "Biologic False Positive Serologic Tests for Syphilis", *J.A.M.A.*, 150: 467.

MORGAN, A. D., and RAVEN, R. W. (1952), "Sjögren's Syndrome, a General Disease", *Brit. J. Surg.*, 40: 154.

MORGAN, W. S. (1954), "The Probable Systemic Nature of Mikulicz's Disease and its Relation to Sjögren's Syndrome", *New England J. M.*, 251: 5.

MORTENSEN, V., and GORMSEN, H. (1952), "Lupus Erythematosus Disseminatus (Libman-Sacks Disease)", *Acta med. scandinav.*, Suppl., 266: 743.

MOTULSKY, A. G., WEINBERG, S., SAPHIR, O., and ROSENBERG, E. (1952), "Lymph Nodes in Rheumatoid Arthritis", *Arch. Int. Med.*, 90: 660.

MYERS, G. B., GOTTLIEB, A. M., MATTMAN, P. E., ECKLEY, G. M., and CHASON, J. L. (1952), "Joint and Skeletal Muscle Manifestations in Sarcoidosis", *Am. J. Med.*, 12: 161.

RAMAGE, J. H., and KINNEAR, W. F. (1956), "Keratoconjunctivitis Sicca and the Collagen Diseases", *Brit. J. Ophth.*, 40: 416.

REICH, N. E., and REINHART, J. B. (1948), "Dermatomyositis Associated with Hypertrichosis", *Arch. Dermat.*, 57: 725.

SHEARN, M. A., and PIROFSKY, B. (1952), "Disseminated Lupus Erythematosus", *Arch. Int. Med.*, 90: 790.

SHELDON, J. G. (1939), "Sjögren's Syndrome Associated with Scleroderma of Legs", *Proc. Roy. Soc. Med.*, 32: 255.

SHIPTON, E. A., and D'OMBRAIN, A. (1949), "Sjögren's Syndrome: Report of a Case with Discussion as to Cause", M. J. AUSTRALIA, 2: 679.

TALBOTT, J. H., and FERANDIS, R. M. (1956), "Collagen Diseases", Grune & Stratton, New York: 141.

WEBER, F. PARKES (1947), "Rare Diseases and Some Debatable Subjects", 2nd Edition, Staples: 16.


## Reviews.

**The Essentials of Modern Surgery.** Edited by R. M. Handfield-Jones, M.C., M.S., F.R.C.S., and Sir Arthur E. Porritt, K.C.M.G., C.B.E., M.A., M.Ch., F.R.C.S.; Fifth Edition; 1957. Edinburgh and London: E. and S. Livingstone, Limited. 9½" × 6¼", pp. 1282, with 649 illustrations. Price: 75s.

THE appearance of the fifth edition of Handfield-Jones and Porritt's "Essentials of Modern Surgery" reflects the continued use of this undergraduate text-book. Situated as it is in a highly competitive field, it may be properly considered both on its own merits and also in relation to the other well-known London text-books.

In 1200 rather small pages, liberally sprinkled with illustrations, it sets out to supply the essential requirements of the undergraduate student in all the divisions of general surgery. Where such compression is necessary, it is pertinent to inquire whether this is better achieved by limitation to elementary standards, or by attempting to condense into a small compass the salient features of the various diseases covered. Both methods are employed in these pages; for whereas the specialist contributors have usually followed the second method with considerable success—and sometimes, as, for example, Holmes Sellars on chest diseases, brilliantly—the principal authors, except with regions in which they are obviously interested, such as the urinary tract, have been content with elementary presentations. These chapters seem even less impressive in relation to the specialist contributions on account of a loose and unprecise style, which is wasteful of space.

In an elementary text-book, because of the uninformed readers for whom it is intended, accuracy of statement is essential. In a number of instances this is lacking. Thus, in the chapter on general surgical technique, advice is given to boil instruments in water for ten minutes, or if they have been used in a septic case, twenty minutes. The acceptance of such advice might well involve a surgeon in a successful action for negligence. It would have been much wiser to insist either that instruments must be exposed to a temperature of 120° C., or that the water must be so treated with appropriate chemicals as to ensure destruction of spores. The use of superheated steam in autoclaves is mentioned as an ideal method of sterilization, but no pressures or temperatures are given; instead, the dangerous advice is offered that if these are not available, lower pressures (than what?) are as efficient though not so rapid (as what period?).

Seventy-two hour skin preparation, preceded by shaving, is still advocated, though it must be at least thirty years since the neurosurgeons showed that this conflicted with elementary principles in the prevention of sepsis, and was far less likely to produce a sterile skin surface than immediate pre-operative shaving and skin preparation only.

Some advice as to treatment is very old-fashioned, to say the least. In acute lymphangitis, the advice to use Bier's hyperæmia, to apply linseed poultices, and to secure free diuresis and copious bowel evacuations might have been cordially approved by Dupuytren; but surely this method has rarely been recommended in the intervening century.

In the discussion on the surgical treatment of duodenal ulcer, though vagotomy receives no mention, loose writing appears in consecutive sentences. Gastro-jejunostomy is said to be fraught with so many serious after-effects that few surgeons practise it today; in fact, it has only one disadvantage—the liability to stomal ulceration. In the next sentence, in reference to partial gastrectomy, the statement is made that any operation is probably useless unless it removes such a portion of the acid-secreting mucous membrane as will permanently relieve the patient of any risk of hyperchlorhydria; in fact, no successful partial gastrectomy does this, but its effect must be regarded either as empirical, or as due to removal of the gastrin-secreting mucosa.

The chapter on the biliary system will give little enlightenment to the curious student.

Defective editing is noted when the treatment of sciatica due to lumbar disk protrusion is discussed. In the section on diseases of the spine and spinal cord, Handfield-Jones writes that in the past laminectomy with removal of prolapsed tissue was practised, but the results were far from satisfactory; however, in a good chapter on deformities, Mercer states that the operation is usually successful, and there are few complete failures.

Though these criticisms seem proper, it can still be stated that this is a beautifully produced book, well printed on good paper, with many appropriate illustrations, and completely free from printing errors. It cannot be regarded as the best book in its field; but for the undergraduate student who derives much of his knowledge from other sources, this book will provide a good grounding in essential surgery.

**A Companion in Surgical Studies.** By Ian Aird, Ch.M., F.R.C.S., and the Staff of the Department of Surgery, Postgraduate Medical School; Second Edition; 1957. Edinburgh and London: E. and S. Livingstone, Limited. 9¼" × 7¼", pp. 1314, with two illustrations. Price: 84s.

WHEN the first edition of Ian Aird's great work appeared in 1948, its concise exposition of an enormous field of knowledge, and its un-English erudition and completeness, made its success with post-graduate students and practising surgeons a foregone conclusion. The constant use of this book in the intervening years has rarely failed to demonstrate that, whatever misnamed encyclopædic work in any number of volumes had already been consulted, Aird would provide a more complete and accurate statement, couched in clear and concise language, and absolutely free from padding.

The rapid advances which surgery has made since 1948 have made a revision inevitable, and in this second edition references are made to nearly 2000 papers published since 1950. The references are said to be complete to August 1, 1956.

This new volume has the same great virtues and the same minor blemishes as the earlier edition. Its virtues are indeed manifold. It is the only truly encyclopædic surgical text-book written in English, and within its limits (orthopædics being excluded) no rarity seems to have been omitted. It might be a just criticism that the very fact of rareness had been made an indication for comprehensive description, sometimes in pronounced contrast to the handling of more common conditions, were it not that the editor stresses in his introduction that this is an academic text-book, serving as a spring-board from which the reader may leap into the realities of clinical surgery, or into the nearly immeasurable repository of observation and deduction in medical literature.

Of necessity the book must be largely a compendium of the views of innumerable authors, though to a considerable extent these are modified by Aird's personal experience. Perhaps because of this, and because the author of such a book is likely to be attracted rather to the academic than to the clinical approach, where the subjects under discussion are sufficiently ordinary for the average reader to have some personal knowledge of them, he may well be inclined to criticize the content of some of these presentations. Most Australian surgeons, for instance, would be critical of the chapter on the gall-bladder and bile ducts, of which it may be said that, apart from the unlikely event that these diseases differ in character as between England and Australia, the presentation is more likely to confuse than to enlighten the post-graduate student. Instead of describing the clear progression from primary gall-stones, to acute obstructive (chemical) cholecystitis, to post-inflammatory gall-stones, and then to repair, Aird describes these diseases with a constant bias towards bacterial infection, whether in relation to the formation of gall-stones, to acute cholecystitis, or to the rubbish-heap termed chronic cholecystitis. Even the description of biliary colic as an intermittent rather than as a constant pain will find only rare confirmation at the bedside.

In the discussion of inguinal hernia, the certainty with which the oblique varieties are regarded as of congenital origin conflicts with modern surgical opinion.

The treatment of desmoid tumour contains no reference to the value of radiotherapy in this condition.

Though references are said to be complete to August 1, 1956, many statements, especially in relation to fatality rates, refer to much earlier periods. Thus the mortality of super-radical amputation of the breast is said to exceed 10%, although large series with a fatality rate less than 1% had been published prior to this date.

To sum up, this is a magnificent work of erudition and scholarship, deserving the thanks of the whole surgical profession. The second edition is even better than the first, and must be an indispensable book for all practising surgeons and for candidates for higher surgical degrees; it can be heartily recommended also to the ambitious undergraduate student.

## Books Received.

*[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]*

"An Atlas of the Commoner Skin Diseases: With 153 Plates Reproduced by Direct Colour Photography from the Living Subject", by Henry C. G. Semon, M.A., D.M. (Oxon.), F.R.C.P. (Lond.); revised with the collaboration of Harold T. H. Wilson, M.A., M.D. (Cantab.), M.R.C.P., D.T.M.; Fifth Edition; 1957. Bristol: John Wright and Sons, Limited. 9¼" × 7¼", pp. 384. Price: 105s.

The previous edition was published in 1953.

"The Breasts and Breast Feeding", by Harold Waller, M.B., B.Ch. (Cantab.), F.R.C.O.G.; 1957. London: William Heinemann (Medical Books), Limited. 7¼" × 4¾", pp. 64, with 16 illustrations. Price: 7s. 6d.

For midwives, nurses, health visitors, general practitioners and obstetricians.

"Obstetric Practice", by H. Bruce Williams, M.B., Ch.M., F.R.A.C.S., F.R.C.O.G.; 1957. Sydney, London, Melbourne, Wellington: Angus and Robertson. 7¼" × 4¾", pp. 174, with illustrations. Price: 25s.

The author states that this is not a usual text-book of obstetrics, but "rather an endeavour to discuss the diagnosis and treatment of the complications which may confront a doctor during pregnancy and labour, and to state when and how to interfere".

"Experimental Psychopathology", edited by Paul H. Hoch, M.D., and Joseph Zubin, Ph.D.; 1957. New York and London: Grune and Stratton. 8½" × 5½", pp. 288, with illustrations, tables and graphs. Price: $6.50.

The proceedings of the forty-fifth annual meeting of the American Psychopathological Association held in June, 1955.

"The Principles and Practice of Diathermy", by Bryan O. Scott, M.R.C.S., L.R.C.P., D.Phys.Med.; 1957. London: William Heinemann (Medical Books), Limited. 8½" × 5½", pp. 200, with 146 illustrations. Price: 25s.

Designed as a text-book for students of short-wave therapy.

"Study Group on Pædiatric Education: Report", World Health Organization Technical Report Series No. 119; 1957. Geneva: World Health Organization. 9¼" × 6¼", pp. 20. Price: 1s. 9d.

The report of a study group which met in July and August, 1956.

The Medical Journal of Australia

SATURDAY, JUNE 29, 1957.

*All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.*

*References to articles and books should be carefully checked. In a reference the following information should be given: surname of author, initials of author, year, full title of article, name of journal, volume, number of first page of the article. The abbreviations used for the titles of journals are those adopted by the Quarterly Cumulative Index Medicus. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.*

*Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.*

## ROAD ACCIDENTS AS A MEDICAL PROBLEM.

THE prevention of motor vehicle accidents on the road is, in many major respects, a medical problem, and is a proper subject for consideration, both by the organized medical profession and by its individual members, in accordance with their special training and interests. The Federal Council of the British Medical Association in Australia, at its meeting in August, 1956, asked the World Medical Association that the matter of road accidents be considered from the preventive medicine aspects. The question was brought forward at the Tenth General Assembly of the World Medical Association in October, 1956, and the following decision was recorded:

> Whereas, the death and maiming of humanity throughout the world is increasing each year; and
>
> Whereas, it is the duty and responsibility of the medical profession in every country of the world to assist in the preservation and maintenance of human life;
>
> Therefore, be it resolved, that The World Medical Association recommend to its member associations that they cooperate with other agencies and authorities within their countries in whatever degree is possible and necessary in a concentrated endeavour to save and preserve human life.

Many people will feel that this was an inadequate way of dealing with the situation, which might well be regarded as a world-wide problem; and it is interesting and a little chastening to learn that, according to S. E. Miller,[1] the United Nations has been interested in the subject of motor vehicle accidents for several years, and has an expert advisory panel on highway accidents and safety, with an expert medical consultant group assembled by the World Health Organization. However, the World Medical Association has thrown the ball back into our court, and at its meeting in February, 1957, the Federal Council[1] discussed the matter fairly fully. The Council of the Victorian Branch of the Association has always been particularly interested in this subject, and one of its representatives at the Federal Council meeting, Dr. Robert Southby, advocated the need for vigorous local action. He pointed out that the problem of road accidents had many medical aspects in which the medical profession was entitled to be interested. The Federal Council then decided to approach the Federal Minister for Health, requesting him to give consideration to the magnitude of the problem of deaths and invalidity caused by road accidents, and earnestly requesting that he give the matter his consideration from the aspect of preventive medicine. It was decided further to inform the Minister that the Federal Council would be willing to cooperate by the formation of a committee sponsored by the Commonwealth Government to collect detailed information on the problem.

It may be held by some that this question of accidents on the road has little to do with the medical profession, apart from the patching-up process. This idea should be completely dispelled by examination of 12 articles which appeared in *The Journal of the American Medical Association* of January 26, 1957. Ten of these articles were read in a panel discussion on medical aspects of crash injuries at the annual meeting of the American Medical Association in June, 1956, one was read at a meeting of the Section of Orthopædic Surgery at the same annual meeting, and one is an independent contribution. Altogether these papers provide a remarkable amount of constructive material, which shows just how widely and deeply the medical profession is involved in this business of road accidents and their prevention. We hope that many of those who are or should be interested in this problem will read them in full. Reference to only a few points is possible here. In considering some general medical aspects of the subject, F. D. Woodward states that something has been achieved in that, despite an increase in the absolute number of fatal automobile accidents per year in the United States, there has been a substantial decrease in the number of deaths per million miles of travel. However, much more can and should be done. Speed and drunken driving stand out above all the rest of the causes, and these should be fought in every way possible. To this end Woodward suggests that it is necessary to overcome the apathy of the public, the legislators and judges in traffic courts by education, and also to have adequate and stricter laws enacted. However, as he points out, there appears to be little likelihood of accomplishing radical changes in human nature in general and exuberant youth in particular, so "it would seem the part of wisdom to work for desirable alterations in the machine itself rather than to place all efforts in an attempt to bludgeon 'old Adam' into safer driving practices". Many suggestions have been made for the redesigning of motor vehicles on safer lines, in addition to the provision of safety belts and body harness, and Woodward states that many motor-car manufacturers are now studying the problem and installing safety devices on their cars. Manufacturers are, of course, not unreason-

[1] *J.A.M.A.*, January 26, 1957.

[1] M. J. AUSTRALIA, April 6, 1957.

ably concerned with sales, and no doubt the general outlook on the subject will need to be changed by public education. Woodward expresses the heart of the matter in one sentence: "If, instead of size, horsepower, acceleration, and speed, the installation of such safety devices can be made the basis of competition, the many people and agencies responsible for this happy event can sit back and applaud." Otherwise legislation will need to be introduced, covering minimum safety requirements. Woodward also advocates the setting up of a National Automotive Safety Foundation to study all phases of automobile crashes. He stresses the importance of a study of these matters from the medical point of view, in an effort to prevent them and further reduce the injuries. He points out that no statistics are yet available on the number of crashes caused by medical conditions. To this end the American Medical Association is directing a study of the medical aspects of automobile crashes, the licensing of drivers and the examination of repeated offenders. This study includes a review of visual, hearing and physical requirements for those holding a licence, of the incidence of Ménière's disease, *petit* and *grand mal* and other diseases of the nervous, cardio-vascular and musculo-skeletal systems, and of the effects of various physical conditions, drugs, insulin shock and alcohol. This is something which might well engage the interest of a medical committee in our own country.

Various important aspects are brought forward by other contributors to the panel discussion. DuPont Guerry III discusses the degree of visual competence required of applicants for unrestricted driver's licences and the wealth of data that might be obtained from screening programmes. He suggests that drivers who have had several accidents should be especially studied. Another question of interest to the ophthalmologist, to which he refers, is the optical properties of windscreens and other details of automobile design that make for distortion, glare and confusing reflections. He states that the problem of visual disturbances induced by faulty design of motor-cars has been a sore spot with manufacturers for many years, and they have all been guilty of sometimes allowing style and so-called beauty of design to overrule safety and functional efficiency. As he puts it, they have allowed the stylists to decide first what would catch the public's eye, and the car then to be built with this in mind. The otologist's point of view is presented by Laurence R. Boies, who discusses two otological disorders that can prevent normal performance of the driver of a motor vehicle. One is impairment of hearing to a degree that definitely handicaps the driver; the other is a disorder of the physiology of the semicircular canals sufficient to make him subject to sudden attacks of vertigo. Prospective drivers should be examined adequately to establish the presence of a disability of this kind. It is, in fact, in their own interests that this should be done, as a competent medical examiner may pass a person who would be rejected by those working on rule of thumb. For example, Boies states that to be a handicap for ordinary purposes, deafness must be bilateral; if the hearing in one ear is normal, severe or complete deafness in the other is not a significant handicap. Moreover, the medical examiner can often establish that a condition such as Ménière's disease is under control, and that the applicant will be a safe driver. Jacob Kulowski brings forward the need for better ways of determining and maintaining the fitness of people who drive motor-cars from the orthopædic point of view. He points out that if patients ask their doctor if it is all right for them to drive, the question cannot be dismissed or evaded; it must be carefully answered for each individual on the basis of clinical experience, common sense and whatever data may be available at present with regard to the connexion between physical disabilities and accidents. He refers to various conditions of interest to the orthopædist, as well as to the presence of plaster casts, artificial limbs *et cetera*, which may either affect the driver's efficiency or increase his susceptibility to injury in the event of an accident. The human factor from the psychological and psychiatric aspects is discussed by R. A. McFarland. He mentions the question of accident-proneness and "the accident repeater", clinical study of whom has led to the hypothesis that "a man drives as he lives". It is obvious from this discussion that a great deal more needs to be known about this side of the question before dogmatic statements can be made. A record of something actually achieved is given by H. Brandoleone, who cites a notable reduction in the annual rate of accidents (from 6377 in 1946 to 3130 in 1955) achieved by a metropolitan transport system by developing a medical programme for drivers and introducing psychological tests. Brandoleone states that the data show that the cost of maintaining a medical department for each year is less than the cost of one bad accident. He provides details of the methods that they have used in this controlled field. S. E. Miller, after considering standards for those applying for permits to drive, makes the startling, yet far from unreasonable, comment that the public should be educated to think of driving as a privilege, not an inherent right as it is regarded today. The public also should be conditioned to accept more stringent qualifications for driving motor vehicles, such as those now accepted for flying a plane, for carrying a gun, or for the practice of medicine or the practice of law.

These are a few odd points; but there is a great deal more in these articles for those who will take the trouble to read them. F. H. Mayfield puts the position concisely and vividly: "As each additional motor vehicle leaves the assembly line, the space on the highway between it and other cars is narrowed, and it seems inevitable that crashes will occur." Both in the prevention of such crashes and in the prevention of injury when crashes do occur, as well as in the efficient immediate and subsequent care of those who are injured, the medical profession can and should have a great deal to say. It is to be hoped that the Federal Council's resolution of last February will achieve something positive.

## Current Comment.

### INTRAVASCULAR CLOTTING.

DESPITE the refinements of knowledge of the factors affecting blood clotting in general, the problem of intravascular clots continues practically to be a vexing one. For this and other reasons much interest attaches to a recent review by A. J. Quick,[1] in which he suggests a

[1] *Angiology*, October, 1956.

probable mechanism of intravascular clotting as based on current knowledge.

Coagulability of the blood is intangible, and as such not capable of measurement. The nearest applicable tests are the determination of clotting time and the prothrombin consumption test; but even so, the former is very often unsatisfactory as an aid, and the latter furnishes no information about the actual completeness of the intracorporeal clotting reaction. Quick and his colleagues have shown that only a trace of thrombin suffices to clot blood completely in a test tube, and that negligible prothrombin consumption occurs in the unretracted clot. In fact, the amount of thrombin able to be produced from one millilitre of blood would be sufficient to clot all fibrinogen present in the circulation. It is, therefore, imperative that some agent be present to remove thrombin expeditiously from serum or to delay its participation in the cyclic reaction that produces more thrombin. In the absence of thrombin, the various clotting factors can coexist without demonstrable tendency to interact. Damage to the endothelium of the vessels, *inter alia*, liberates thromboplastin. The amount of thrombin need not be large, since, besides clotting fibrinogen, it activates the thromboplastinogen complex, which then reacts with platelets to form thromboplastin. So more prothrombin becomes available to thrombin, and a potentially highly dangerous chain reaction is begun. Thus, the first line of defence is fibrin, which adsorbs thrombin quickly and holds it tenaciously. Its reticulated structure in clot offers a large surface to the dispersed serum; its instantaneous avidity for thrombin prevents the autocatalytic reaction. The second line of defence is the naturally occurring $\alpha$-globulin, antithrombin, a cofactor of heparin. It has a high neutralizing capacity, but its action is slow. Heparin does not appear to play a cardinal role here. If fresh thrombin-rich serum is injected into the dog, no intravascular clotting occurs, but blood samples taken up to forty minutes after this will still clot on standing even if immediately mixed with sodium oxalate at that trial. Apparently the antithrombin-thrombin complex allows the liberation of small amounts of free thrombin, but heparin secretion is not stimulated.

Why does the blood remain fluid? All the clotting factors are in an inactive state and cannot be activated autocatalytically or by each other. Thromboplastin is required for prothrombin conversion to thrombin, and it is absent from blood itself. For thromboplastin formation, platelets must interact with thromboplastinogen and several other factors, such as plasma thromboplastin, antecedent and component, in the presence of thrombin. The last-mentioned is thought to be necessary because lysed platelets can be injected intravenously with impunity, and a concentrate of platelets will react only if the plasma factors are first activated by thrombin. Most of the primary clotting factors are much in excess of minimum requirements, and the coagulability of the blood is not affected within wide limits of concentration differences. Thus antihæmophilic globulin can be reduced to 5% of the normal amount without change in clotting time.

Formation of an intravascular thrombus would thus require some damage for release of thromboplastin from vascular endothelium, immediate thrombin generation and formation of a small clot at the site of injury. When clot retraction occurs, a serum rich in nascent thrombin is expressed. Rapid dilution in a free-moving circulation presumably would render this innocuous; but if the stream is stagnant, this thrombin-rich serum will clot more fibrinogen, bringing about formation of a secondary clot attached to the original thrombus. By repetition a very long clot may be formed. (There is no discussion of the dilution postulated here, although it is obviously of importance, as it has already been stated that only small amounts of thrombin need be present to keep the clotting process going.)

As clot retraction is thought to play a key role, factors influencing this are enumerated. The number and quality of the platelets are in some instances thought to be related to thrombosis. Quick suggests that the relatively high incidence of thrombo-embolism after splenectomy may be related to the sudden rise in the number of platelets often occurring after this operation. The influence of fibrinogen on thrombosis is a relatively unpondered problem. Quick has shown that clot retraction decreases as the concentration of fibrinogen increases. This would mean a decrease in thrombosis with high fibrinogen levels and perhaps an increase in thrombosis with low levels. Further, *in vitro*, the addition of increasing amounts of thrombin to constant mixtures of platelets and fibrinogen leads to greater and speedier clot retraction. The rate of thrombin formation may in part be exerted on clot retraction and supplies an explanation of action of substances such as dicoumarol. This depresses prothrombin production so that thrombin generation is greatly decreased. Intravascular clot retraction is greatly delayed, and whatever serum escapes is so poor in thrombin that secondary clot formation does not occur. This explains why dicoumarol is effective despite the fact that clotting time is very little prolonged. Clot retraction increases as the red cell volume decreases, but the evidence that thrombosis increases with anæmia is poorly documented. It is obvious that these factors would make good grounds on which to test the importance of the clot retraction hypothesis. None is sufficiently worked on to provide an answer.

Finally, consideration is given to phenomena in which a marked decrease in fibrinogen and other clotting factors occurs in conditions in which overt signs of intravascular clotting are usually lacking, but in which thrombosis would seem to occur. Thus, in premature separation of the placenta and retention of a non-viable fœtus, severe hypofibrinogenæmia often occurs. At present this is considered to be due to entrance of thromboplastin from the placenta into the maternal circulation with widespread, if clinically occult, clotting. The deposited fibrin disappears apparently from fibrinolysin. Fairly similar is the reaction following transfusion of incompatible blood characterized by massive lysis of red cells, thrombocytopenia, hypoprothrombinæmia and hypofibrinogenæmia. The red cells as well have been shown to contain a potent clotting factor, not requiring thrombin, which acts directly on the thromboplastinogen complex to form thromboplastin. The subsequent low levels of the clotting factors that follow this reaction suggest that massive (widespread) thrombosis has occurred, but it occurs without any local clinical evidence.

## DR. SAMUEL ADAMS AND HIS DIARY.

THE broad stream of recorded history is augmented by many small sources. Not the least valuable of these is the diary kept by an observant and intelligent person, who is not content simply to note the events important to his own personal affairs, but has a wider vision, and leaves for posterity a homely and human account of contemporary life. As R. Scot Skirving[1] put it:

> The world would have been poorer if Samuel Pepys's too short a diary had not been discovered and interpreted. Again with all its looseness William Hickey gave us an unforgettable picture of Anglo-Indian life in the late eighteenth and early nineteenth centuries. No full story could be written of the struggle between Britain and France for the prize of Hindustan without the help of this amusing old dog's book of memory.

Thomas M. Hunter[2] has told the story of Dr. Samuel Adams, "Revolutionary Army Surgeon and Diarist", chiefly from Dr. Adams's own diary, which he began on March 12, 1758, at the age of thirteen years, and concluded on February 25, 1819, nine days before his death at the age of seventy-four years. Seldom can there have been such an inveterate recorder of small as well as of important happenings. Samuel Adams's life was eventful enough in all conscience, although he was not the Sam Adams of Boston Tea Party fame. He was, however, almost as intimately connected with Revolutionary politics, and was as faithful a servant of developing medical science. In

[1] M. J. AUSTRALIA, October 2, 1954.
[2] *U.S. Armed Forces M. J.*, May, 1957.

his time American medicine was far below the status of European medicine. The apprenticeship system was the usual method of training, and even boys of good family who studied medicine in that way had to do menial tasks and often, as in Adams's case, tend the apothecary's shop which was an adjunct of the doctor's surgery. The medical department of the University of Pennsylvania was founded in 1765, the Massachusetts Medical College (Harvard) in 1782. Dissections were only rarely performed, and then by stealth. Hospitals were few; there were the Pennsylvania Hospital, founded in 1755 by the efforts of Dr. Thomas Bond, senior, and Benjamin Franklin, and one in New York, destroyed by fire and rebuilt in 1774, but mostly used for barracks. Obstetrics did not become a part of a doctor's studies until after the middle of the century; midwifery was completely a woman's domain. Samuel Adams took a keen interest in obstetrics, and must have acquired great skill; in Ipswich, between 1782 and 1796, he confined 485 women, without once using forceps and without losing a single mother. Although he was born in Connecticut, he spent most of his life in Massachusetts and Maine, and he was called upon as an obstetrician by people far and wide. From 1796 until his death in 1819, he attended 1115 obstetrical patients; all these cases he recorded in his notebook, "Lying-In Cases by S.A.".

The vicissitudes of Samuel Adams's life, though enthralling, are too complicated to be more than summarized here. He began his career as a foot soldier, came under the command of the famous Colonel Phineas Lyman (who greatly influenced his political views), and turned his attention to the study of physick under Dr. Nathaniel Freeman, another ardent patriot. (Freeman, like Lyman, lost his life at the hands of Loyalists.) When he began the practice of medicine in 1769 at Truro, Massachusetts, Samuel Adams adopted the current procedure of bloodletting, extracted many teeth, and constantly prescribed cathartics and diaphoretics for fever, elixirs such as antimony for female disorders, and varied tinctures and cordials for the stomach. He tried to set down in his "Anatomy and Commonplace Book" all the knowledge then available, including many revolting, not to say ludicrous, medical recipes of the day. A few examples are worthy of reproduction:

> Good dung mingled with vinegar and a little bran and applyed as a plaister to a sore breast catcheth wonderfully all swellings thereof.
>
> Stop both your ears with your fingers and the hiccough will go away.
>
> Take Vitriol all two drachms and dissolve it in a pint of clear water and with the water wash the hands it will cure ringworms better & scales in the same.

Perhaps the flourishing sterility clinics of the present day may be interested in the following test of female fertility:

> Let a woman make water in a urinall that is clean upon some barley corns and set the same in a cold place 8 days and if the (illegible) barley corns will grow again then the fault is not in the woman that she conceives not but in the man if otherwise than the fault is in her.

Astrology also played a part in medical practice, as the following shows:

> Let the physician take heed of his first visiting of the sick in the hour of Saturn and Mars if he come to him in the hour of Saturn either the sick will dye or else the physician shall have great labour doubts & (illegible) in the caring of him if in the hour of Mars there will be chidings and brawlings between him & the sick party & shall gain the hours of Jupiter & Venus are much praised the hours of the other planets are indifferent.
>
> He that receiveth a sum of money in the hour of Venus will spend the same with women in pleasure and wantonness.

(Some of the peculiarities in Adams's diary are no doubt due to what Hunter describes as his "painfully diminutive and sometimes obscurantist handwriting, plus occasional code".) In 1775 Adams made the acquaintance of General Washington, whom he frequently saw later, and was appointed an army surgeon. He resigned his commission in 1783, having seen a considerable amount of service, undergone some disillusioning experiences and had much turmoil on the question of his back pay. The fact that he had not received this from the Government was a particularly sore point because he had married his fourth wife, and had a family to provide for. He tried tavern keeping for three years, and finally took up country medical practice at Bath, Maine. Here he became a prominent citizen, and wrote in his diary about "family life, current events, social affairs, his medical practice, work in the kitchen garden, now his main hobby and his fondest, and, finally, the weather, his lifelong interest". In the years 1811 and 1812 he was paid by the town of Bath to be in attendance upon the poor. Here his wife and two of his children died; but Adams may almost be said to have made a hobby of matrimony, because at the age of seventy years he married again. He died in 1819, when his daughter Julia Ann was nine months old.

Hunter records that Samuel Adams was considered "the most intelligent and successful practitioner in the State of Maine" in his day. It was not an easy time for a profession to grow, and medicine was trying to grow to professional status; at the same time America was growing into a nation. Adams's work as an obstetrician and as an army surgeon was skilful and faithful. As a hospital surgeon, he did his best to improve hospital facilities and administration. There was an increasing attempt at the pursuit of science in America, and Samuel Adams was among those making it.

## SOVIET INVITATIONS.

For some time it has been the custom of the Soviet Republic to invite small groups of men, distinguished in some field of expert work, from one country after another and to give the visitors the opportunity to view and examine the methods of teaching and the conduct of research in their specialty. Among the reports of such visits we may refer to two that will interest the medical profession. After the International Physiology Congress in Brussels in July and August, 1956, four American physiologists proceeded to the Union of Socialist Soviet Republics and there studied the elaborate organization which is centred round physiology. A report of this visit has been written by Professor Chauncey Leake,[1] well known especially in this year for his translation of Harvey's *De Motu Cordis* and also for his useful abstracts of current medical literature, which he has conducted single-handed for many years. Professor Leake's account of the tour is severely factual, but he pays a tribute to the cordiality of the hosts and the complete freedom of movement and photography. Physiology, it should be mentioned, is given an emphasis in Russia greater than in any other country—possibly the eminence of Pavlov is largely responsible for this. "The organization of physiological teaching and research in the Soviet Union is complex." Students are taught in some 80 medical schools, which are independent of the universities. Advanced teaching is given in several institutes or in the specialized laboratories of the Faculty of Biology of the University of Moscow. The research institutes are bewilderingly numerous and well equipped. The Institute of Experimental Medicine in Leningrad has a staff of approximately 200 scientists and about 30 graduate students. In Moscow there is the Institute of Normal and Pathological Physiology. Then there is in Leningrad the Pavlov Institute of Physiology (1950) with 200 scientists and 700 technicians. A recent development is the establishment of the Institute of Evolutionary Physiology in Leningrad. In Moscow there is the Sechenov Physiology Institute located in the older buildings of the University of Moscow. Professor Leake gives details of the various researches being carried out during the American visit, and certainly the list is an imposing one. Russian physiologists take a wider and more inclusive view of the scope of their science, rather reminding one of the attitude of J. W. Draper, who declared that his

[1] *Science*, September 21, 1956.

history of the intellectual development of Europe was a chapter in his text-book of human physiology. The only suggestion of criticism in Leake's account is to be found in the statement that Soviet physiology "seems generally to be channeled into detailed extension of the Pavlovian canon". Later in the report he comes back to this theme: "Soviet physiologists are keen workers and thinkers however closely they may be oriented toward the Pavlovian canon." Now Russian physiologists have every right to be proud of the far-reaching discoveries of Pavlov, but they are apt to allow their admiration to inhibit criticism, for Pavlov in his later years put forth opinions which western biologists were unable to accept, such as the hereditary transmission of acquired characters; even his earlier work, which led him to postulate an intimate and detailed adaptation of digestive juices to their food substrates, was widely challenged.

The other report of value is that given by four French surgeons who were invited to inspect hospitals, teaching of students and surgical technique.[1] This report will be accepted as a singularly detached and candid finding. The description of the medical curriculum pursued by students is well worthy of careful study, and valuable hints are certain to be gained. Everywhere energy and enthusiasm were evident, and plans for the future were of the long-range type—all this is faithfully recorded and extolled. The four French visitors were greatly impressed by some films, one showing the transplantation of a heart into another animal, another the grafting of the head of a small dog onto the neck of a larger dog by suturing one carotid artery and one jugular vein. Concerning the general conditions of surgical technique and of the standards of hospitals, the visitors found a curious mixture of the old and the new. The hospitals, which are candidly described as "mediocre", reeked of antiseptics; instruments, all made in Russia, included the obsolete as well as the very modern. The cleanliness and organized efficiency characteristic of American hospitals were not evident, though many improvements were being carried out and many planned. Physiological considerations were given more emphasis than in other lands throughout the wide range of diagnosis, treatment and research. The authors conclude: "Our professional contacts were very numerous. . . . But never did we visit the homes of our colleagues, never did we learn anything of family life and extra-professional activities . . . the doors which led to private life were never opened."

The question may be asked if these invitations to the Soviet Union should be accepted. The answer is surely that they should: courtesy must be met with courtesy, and the certainty of learning something of moment must be kept in mind. But let visitors of British and American upbringing and tradition keep in mind the old English proverb: "It is a sotill mowse that sleepeth in ye cattis ere."

## A FOLLOW-UP STUDY OF FRONTAL LOBOTOMY.

FRONTAL LOBOTOMY, when it was first introduced, met with suspicion and hostility, and over the succeeding period has been viewed with misgiving by many; feelings have ranged from great enthusiasm to unqualified opposition to its use. However, it has had a fair trial, and it is useless to deny that in selected cases the results from this operation, in one form or another, have been valuable and, at times, brilliant. Few, if any, surgeons have had more experience in this field than Walter Freeman,[2] who has reported a study of some 3000 patients subjected to one type or another of lobotomy by himself or under his direction over the past twenty years. The period of follow-up of these patients varies from one to twenty years. Freeman states that in the study the question of social adjustment has been uppermost in his mind. The impact of psychosurgery upon the hospital population has been dealt with, rather than the effect of operation upon individual patients. The questions were asked whether the application of lobotomy and kindred procedures could make a dent in the rising curve of hospital population, whether the restoration of a large number of patients to the community brought with it major difficulties in the domain of the family and the community, and whether the effects of psychosurgery were limited to a few months or years, with an inevitable return to hospital existence.

The material examined is in two main divisions: a series of 600 patients who underwent pre-frontal lobotomy and another series of 2400 patients who underwent transorbital lobotomy. A comparison was also made between private patients and State hospital patients, and a further subdivision was made according to personality reaction type—schizophrenic, affective and psychoneurotic. The studies reveal that as a result of prefrontal lobotomy some 70% of schizophrenic subjects, 80% of affective subjects and 90% of psychoneurotic subjects are carrying on outside hospital in a follow-up period of five to ten years. A dissection of the figures reveals that the useful result is twice as high in private patients as it is in State hospital patients. Comparison shows that transorbital lobotomy is safer, more effective (apart from hallucinated schizophrenic patients) and far more readily applicable to the problem of the State hospital than is pre-frontal lobotomy. Study of the relapse rate and of the performance of multiple operations reveals that 300 patients of the 3000 have undergone more than one lobotomy with substantial benefit—that is to say, the ability to live outside the hospital—in a third of the cases. At the same time the long-range study shows that the relapse rate is almost balanced by the delayed recovery rate. Some patients have left hospital five or more years after operation, and others, at first house-bound, have resumed employment or housekeeping even after a ten-year post-operative period. Freeman states that prognosis in psychosurgery rests more firmly upon the duration of hospitalization than upon any other factor. While there are some extraordinary patients who make a substantial social recovery after a decade or more spent in hospital, these are so few that they become negligible in the study of large numbers of individuals. Nor is the opposite true, that every patient with a disabling psychosis or psychoneurosis will recover if operated upon early in the course of his illness. Some patients progress from the beginning of their psychosis, and within months or even weeks are beyond medical, psychotherapeutic or surgical aid. These are also in the minority, but their presence is recognized.

One interesting comment made by Freeman is to the effect that hospitals which select patients for operation with a view to release, and which encourage the relatives of patients to participate actively in the management of convalescence, enjoy a much higher percentage of released patients than do those that employ lobotomy more for the control of disturbed behaviour. This is an important point in the light of Freeman's particular concentration on the impact of psychosurgery upon the hospital population. However, he does make some encouraging reference to individual results, and points out that high-level performance is possible after major pre-frontal lobotomy, and especially so after transorbital lobotomy. This, he states, is indicated by the competence of lobotomized patients in such professional fields as medicine, law, teaching, nursing and others. One patient is a member of a first rate symphony orchestra; another is functioning well as a missionary in the Far East; a psychiatrist was promoted to chief of service in a large mental hospital; a fourth is confidential secretary in "a sensitive spot" in the United States Federal Government. Freeman points out that such individuals are in the minority, but the same can be said of other individuals whose frontal lobes have never been operated upon; he also emphasizes the fact that no patient was subjected to lobotomy unless faced with disability or suicide and until reasonable trial of other methods of treatment had been applied. The value of these results cannot be gainsaid, whether or not frontal lobotomy is completely displaced in the future by some less drastic form of treatment.

[1] *Presse méd.*, February 23, 1957.
[2] *Am. J. Psychiat.*, April, 1957.

# Abstracts from Medical Literature.

## DERMATOLOGY.

### Subcorneal Pustular Dermatosis.

I. B. SNEDDON AND D. S. WILKINSON (*Brit. J. Dermat.*, December, 1956) report a series of cases of subcorneal pustular dermatosis. The main feature of these cases was the onset in middle life of a recurrent vesico-pustular eruption which ran a harmless but protracted course over a number of years. All but one of the six cases described were in women, and the average age of onset was 54·8 years. The duration of the disease varied from three months to nine years. The axillæ, groins, abdomen and flexor aspects of the proximal parts of the limbs were particularly affected. The hands, feet, face and mucous membranes were entirely spared. The pustular nature of the eruption, which histological examination showed to be a subcorneal blister filled with polymorphonuclear leucocytes, was a feature of all cases. Diamino-diphenyl sulphone ("Dapsone") was successful in controlling the eruption in four of the six cases. It is suggested that the eruption is distinct from *dermatitis herpetiformis*, though similar in the grouping of the lesions, in its protracted course and in its response to remedies.

### Pyoderma Gangrenosum.

H. O. PERRY AND L. A. BRUNSTING (*Arch. Dermat.*, March, 1957) report the clinical and laboratory features of 19 cases of *pyoderma gangrenosum*. In 11 cases clinical and laboratory evidence of ulcerative colitis was present. It would appear that *pyoderma gangrenosum* is not invariably associated with disease of the bowel. An element of hypersensitivity characterized the patients. Lesions are commonly provoked by trauma to the skin, and untoward reactions to the injection of iodides may occur. No form of treatment of *pyoderma gangrenosum* is effective unless the underlying disease process is also controlled. In patients with ulcerative colitis, and also in others in whom no such process could be demonstrated, the use of salicylazosulphapyridine ("Azulfidine") in long courses was the most effective of all forms of treatment. No one specific medication for the treatment of *pyoderma gangrenosum* has been available. The dosage of salicylazosulphapyridine usually employed was 0·5 gramme every three hours for seven or eight doses during a twenty-four-hour period. In maintenance therapy, if necessary, it was suggested that the drug be taken for ten days alternating with a ten-day rest period.

### The Role of Pseudomonas Aeruginosa in Infections About the Nails.

M. F. BAUER AND H. COHEN (*Arch. Dermat.*, March, 1957) state that *Pseudomonas aeruginosa* has been accepted as the causative agent in certain cases of external otitis, *otitis media*, meningitis, septicæmia and infantile diarrhœa, and in some genito-urinary infections. It has seldom been considered as more than a secondary invader. The authors have studied four cases in which it was difficult to relegate the role of *Ps. aeruginosa* to that of a secondary invader. The infection began about the nail in all cases. Good therapeutic results were obtained only when agents were used to which *Ps. aeruginosa* was sensitive. Four cases of infection about the nails are reported. *Ps. aeruginosa* is believed to be the causative agent of these lesions, which on morphological grounds were diagnosed as *acrodermatite continué* of Hallopeau, paronychial infections, and blue-black discoloration of the nail plate. The most effective therapeutic agents appeared to be cool "soaks" of polymixin B sulphate (0·1%) in acetic acid (1%), followed by methylrosaniline (2%).

### Drug Eruption from Rauwolfia Serpentina.

M. S. ROSS (*Arch. Dermat.*, March, 1957) reports an eruption from *Rauwolfia serpentina*. The patient in question received Rauwolfia in the form of reserpine ("Serpasil"), 0·25 milligramme daily for a month, with considerable improvement in her temperament if not relief of her psoriasis. The dose was then reduced to one tablet daily, and the patient continued on this dose for a period of six and a half months. A generalized petechial eruption finally brought her to the office. The eruption developed into hæmorrhagic and ecchymotic areas in some places. Upon cessation of medication, the entire eruption diminished and disappeared.

### Selenium Sulphide Suspension in the Treatment of Tinea Versicolor.

N. E. LEVAN (*Arch. Dermat.*, January, 1957) in five years has treated 23 patients with selenium sulphide suspension (2·5%), the diagnosis in each case having been confirmed by demonstration of the pathognomonic spores. After a shower, the entire body except for the face was to be lathered with the suspension, the latter left on for five minutes, and then the face lathered again for an additional ten minutes. This procedure was to be repeated on each of three successive nights. All patients were reexamined one or two weeks after completion of treatment, and 14 of the patients were followed for a period of six months to two years. Examinations were made under both natural and Wood light. On initial reexamination, one patient showed persistence of the infection. Additional treatment was advised for three patients who showed pin-point follicular yellow lesions under Wood light. No infected areas were seen in the remaining 19 patients. There was a total of five failures. No toxic side effects were noted.

### Isoniazid in the Treatment of Acne Vulgaris.

R. A. OSBORNE (*Arch. Dermat.*, January, 1957) has studied the effects of isoniazid in the treatment of *acne vulgaris*. A group of patients was selected whose acne had been recalcitrant to treatment, and the drug was given daily for periods of one to three months. Some of the patients were helped, a few quite remarkably. The patients selected had moderate to severe acne. All patients were continued on carbon dioxide slush therapy and *Lotio Alba* applied locally. Each patient was given 100 milligrammes of isoniazid three times a day, and a check was made weekly. In all 20 patients were treated; nine had good results. A fair response was shown in two, and in six there was no change in the acne. It was noticed that the patients who benefited were those whose acne had an appreciable erythematous component.

## UROLOGY.

### Isolated Ileal Segment for Urinary Diversion.

J. J. CORDONNIER (*Urologia*, February, 1956) reports on two years' use of an isolated segment of ileum, taken from its terminal part, to subserve urinary diversion. This method has been used in all patients when a reasonably long life expectancy could be anticipated. Ureterosigmoidostomy is reserved for those with a poor life expectancy. Reasons for adopting an ileal segment are the reduced incidence of urinary sepsis, and an absence of hyperchloræmic acidosis. Utilization of the principle was stimulated by the work of E. M. Bricker, who reported a series of 106 such diversions in cases where pelvic evisceration or total cystectomy ha been carried out; in a great majority of his cases the patients had healthy kidneys afterwards, with no hydronephrosis or infection. Length of the segment is about 18 centimetres, and both ureters are implanted into it. The distal end of the segment is brought to the surface half-way between the umbilicus and the anterior superior spine of the right ileum. Urine is collected in an ileostomy bag, which is glued to the skin. A fundamental fact is that the segment is in no way to be regarded as a substitute bladder, or reservoir; it acts simply as a conduit to allow one opening on the surface. Contact of urine with the bowel mucosa is so short in time that reabsorption of electrolytes is only slight. The author's experience so far is 34 cases, with only one post-operative death. Wound dehiscence occurred in three cases, but was not fatal. No clinical peritonitis occurred. Urine output was prompt. Many of the patients showed mild dilatation of the upper part of the urinary tract for four to six weeks post-operatively, but it then subsided. A late complication was a 50% incidence of pyelonephritis, never severe, and easily controlled by antibiotic therapy. However, this does indicate that there is a possibility of progressive renal damage as time goes on. Two patients showed sensitivity to the ileostomy bag. Three required revision of the stoma on the surface.

### Prolonged Treatment of Bilateral Renal Tuberculosis by Antibiotics.

S. PETKOVIC AND V. ILIC (*Urologia*, October, 1956) report from Belgrade their experience with bilateral renal tuberculosis both in the present antibiotic era and before the present chemotherapeutic system was introduced. From 1945 to 1955, 149 patients with bilateral

renal tuberculosis, 53 of whom lived in the preantibiotic era, were followed up. Only five of this group of 53 received antibiotics later on. Of the remaining 48, none of whom received any chemotherapy, not one was living after seven years. An exact report on 101 patients treated by antibiotics is given. In this period (1949 to 1955) only one patient died. However, early in 1956 two other patients died of renal failure. Even then the total mortality rate over the six observed years was only 3%, an enormous improvement. In general, after the method had developed for some time, the doses of each drug were relatively small. PAS was given in doses of 12 to 14 grammes per day, isoniazid in doses of 250 to 350 milligrammes per day, and streptomycin in doses of 1·0 gramme every three days.

### Vascularization of the Prostate.

F. R. BANCHIERI, G. GAMBETTA AND S. MARZOLLA (*Urologia*, October, 1956) have made anatomico-radiographic studies of 50 cadavers of subjects aged between thirty and eighty-two years, to determine variations in the vascular supply of the prostate. The results of these studies show that in many cases the origin of the prostatic arteries is different from that reported in a number of classical studies in the past. For instance, in the report by Flocks in the United States of America in 1937, it was stated that the prostatic artery arose in 100% of cases from the inferior vesical artery. The present authors determined that this was so in only 8% of cases, while the most common origin of the prostatic artery was shown to be the obturator artery. In some cases the prostatic artery arose from the inferior vesical on one side and from the obturator on the other. These findings may prove to be of great practical interest to urologists who desire, by preliminary arterial ligation, to diminish hæmorrhage for the prostatic bed after enucleation of the "adenomatous" mass.

### Fatal Air Embolism During Presacral Air Insufflation.

A. M. LEFKOVITS (*J. Urol.*, January, 1957) states that since 1950, when Ruiz Rivas described it, the presacral method of air insufflation has been fairly widely adopted, and most workers testify to its safety. The method was designed to replace perirenal insufflation, which gave only unilateral results, and could be dangerous. However, the unfortunate case of a male Negro patient, aged only forty-seven years, with suspected phæochromocytoma, who became unconscious during the procedure and died shortly afterwards, has led the authors to review the literature of this diagnostic method. In the case under discussion a post-mortem X-ray examination showed that the perirenal areas were well delineated by the air. Air bubbles escaped from the coronary vessels and the right ventricle at autopsy. There was very advanced coronary artery sclerosis. The author points out that the retrorectal space is avascular, and that therefore embolism is very unlikely. The cause of this air embolism was not definitely determined. The air was injected slowly in amounts of 50 cubic centimetres, and aspiration was carried out repeatedly to make sure that the needle was not in a blood vessel. The presence of a large amount of air in the retroperitoneal space indicates that only a small fraction of the air injected entered the vascular system. It is conjectural whether the air was injected into a vein directly, or whether it entered a vessel as it dissected its way through the retroperitoneal tissues.

### Treatment of Hydronephrosis.

T. E. GIBSON (*J. Urol.*, December, 1956) has revised his ideas for plastic operation upon the ureter. He holds that when conditions are not so unfavourable as to prevent it, the ideal to be aimed at is a plastic procedure about the use of a splint, since it is an irritating foreign body. In addition the nephrostomy drain is better omitted as well, if possible. In addition to the foreign body reaction and the added risk of infection, a third point is that a splinting tube destroys the normal beneficial hydrodynamic effect that the urinary head of pressure should have on the healing ureter. When there has been such destruction that easy approximation by suture is impossible, a splint is necessary as a scaffold to enable the ureter to regenerate about it and so bridge the gap. When possible, a method should be chosen which avoids a transverse circular suture with consequent risk of stricture. This is achieved by using a flap, as in the Foley and the Culp-Scardino procedures. In England, Anderson and Hynes, and in Germany, Bischoff, have been using the same principles successfully. The line of anastomosis should be so fashioned that any subsequent contraction is innocuous. The principle that allows part of the pelvis to be turned down as a flap ensures that the pelvis is drained at its most dependent part. The only provision for drainage is a simple slit or vent in the renal pelvis well above the anastomosis.

### Malakoplakia of the Urinary Tract.

E. F. NATION (*J. Urol.*, November, 1956) states that there is no doubt that malakoplakia is a morphological entity. It is difficult to understand why it should occur much more often in women than in men, unless it is due to the frequency of urinary infection in women. The present reported case brings the total number in the literature to 68. Fortunately, the disease responds readily to antibacterial therapy and electrocoagulation. Malakoplakia is a unique, non-specific inflammatory response of the urinary tract to coliform infection. In the reported cases it has been localized to the urinary bladder. The disease is characterized by yellow or brown submucosal plaques composed largely of macrophages, and often containing Michaelis-Gutmann calcospherite inclusion bodies.

### Phæochromocytoma.

G. F. CAHILL AND E. M. PAPPER (*J. Urol.*, November, 1956) have made a study of 47 cases of phæochromocytoma found in the hospitals of the Columbia-Presbyterian Medical Centre between 1924 and 1956. They state that the course and prognosis of this disease have been profoundly modified for the better in the past ten years by the effective use of catechol-blocking agents and by nor-adrenaline replacement in the early post-operation hypotensive period. General studies of this disease showed that, in earlier periods, the mortality rate after removal of phæochromocytoma was about 25%, while if operation was performed for other pathological conditions (the phæochromocytoma being unsuspected), the mortality rate was over 50%. Therefore, if a phæochromocytoma is believed or known to be present, an operation for any other condition should be postponed until the phæochromocytoma has been either removed or excluded. Ability to diagnose these neoplasms has improved gradually since the first one was found at autopsy in 1924. However, even in a hospital where the syndrome is watched for, the "silent" case still occurs. As yet, the reason for lack of clinical symptoms from the "silent" tumours is not clear, because some of them are found to contain high amounts of catechols, which are released only with operative manipulation. The usual case, however, presents symptoms arising from effects of excess catechols. These are attacks of paroxysmal hypertension in an otherwise normotensive patient, or in a patient with sustained hypertension. The 47 patients in this study comprised 25 paroxysmal hypertensive, nine persistent hypertensive and 15 "silent" types. There were two patients with more than one tumour. In diagnosis, the authors now determine whether or not there is an excess of catechols in the urine, either continuously or in an attack, and then try to locate the tumour by gas insufflation. Once a diagnosis is made, the patient should be studied to estimate any possible damage sustained by the excess hormonal secretion; such effects may be on (i) the cardio-vascular system, (ii) the thyroid metabolic system, (iii) glycogenic metabolism, (iv) fluid and electrolyte balance, and (v) renal function. Blocking agents are used to correct the effects of excess catechols; the most useful of these are "Dibenamine" and "Rogitine", the action of the former being more prolonged; in addition it is an almost complete sympatholytic blocking agent. However, "Rogitine" has been the agent most recently used to prepare the patient for operation and during the operative period itself. It is given in intramuscular doses of 5·0 milligrammes several times a day. At operation, the important thing is to avoid handling the tumour until all its vessels have been ligated. Supporting agents must be ready for immediate use at operation, since all patients have a period of hypotension after the tumour secretion has been cut off from the circulation. The most frequently used anæsthetic was "Avertin" with ether and oxygen. Anoxia must be avoided, because it may cause uncontrollable tachycardia and hypertension, with circulatory collapse. Postural changes are poorly tolerated; therefore the patient is anæsthetized in the position of operation, a transverse upper transperitoneal approach being preferred. As soon as the last of the vascular ligatures has been tied, an infusion of nor-adrenaline is started. The tumour itself is then handled for the first time, separated and lifted out. There has been only one death in the last 26 cases.

# British Medical Association News.

## SCIENTIFIC.

A MEETING of the New South Wales Branch of the British Medical Association was held at the Royal North Shore Hospital of Sydney, Crow's Nest, on April 11, 1957. The meeting took the form of a series of clinical demonstrations by members of the honorary staff of the hospital.

### Syringobulbia.

DR. ERIC DAVIS showed a female patient, aged forty-three years, who, after a normal confinement in May, 1954, had first noticed difficulty in swallowing. About that time she noticed that her voice was husky. The two symptoms varied in intensity, but were persistent. In August, 1954, she had a sudden attack of vertigo one morning, and after that there was deviation of the tongue to the left. About December, 1954, she had a subjective sensation of numbness in the left cheek and pain in the left shoulder. She was admitted to hospital for investigation.

On examination, the patient was not distressed, but she obviously had a weak, husky voice and a weak cough. There was deviation of the palate to the left, and the left vocal cord did not appear to move on phonation. Wasting and weakness of the left sterno-mastoid and left trapezius muscles were also present, and the left side of the tongue was atrophied and fibrillating. The reflexes were not exaggerated; the plantar responses were flexor, and no other signs were elicited in the nervous system.

A number of investigations were carried out, with the following results. A blood count showed that the hæmoglobin value was 13·3 grammes *per centum*, and the leucocytes numbered 5500 per cubic millimetre, 79% being neutrophile cells, 1% eosinophile cells, 19% lymphocytes and 1% band forms. Lumbar puncture produced clear fluid; microscopic and biochemical examination revealed no abnormality, and serological tests gave negative results. The Eagle flocculation test produced a negative response. X-ray examination of the skull revealed *hyperostosis frontalis interna*, with calcification in the right parietal region and a normal appearance in the basal views. X-ray examination of the cervical part of the spine revealed degenerative changes in disk space between the fifth and sixth cervical vertebræ. In a vertebral angiogram, the only significant abnormality noted was that the vertebral artery took an unusually wide swing about the arch of Atlas. Lumbar air encephalography was performed; no definite conclusion could be drawn from the X-ray pictures.

Dr. Davis said that the patient had been shown at a clinical meeting at the Northcott Neurological Centre to Sir Russell Brain, who considered that she might possibly be suffering from early syringomyelia. No treatment was given, and she was to be examined again by Dr. J. M. F. Grant.

### Cerebral Hæmorrhage.

Dr. Davis also showed a married woman, aged forty-five years, who had been in her usual state of health until September 3, 1956, when she had a cerebral vascular accident with signs of an internal capsule lesion on the right side. It was not possible to obtain a history from the patient on her admission to hospital.

On examination of the patient, she was found to have total left hemiparesis, most pronounced in the arm and face. The tongue deviated to the left, and a left upper motor neuron facial nerve palsy was present. The plantar response was extensor on the left side, and the plantar response on the right side was doubtfully extensor. There were no signs of cerebral irritability. Her blood pressure on her admission to hospital was 170 millimetres of mercury, systolic, and 100 millimetres, diastolic, and examination of the other systems revealed no abnormality apart from a palpable swelling above the pubis which was thought to be due to an enlarged uterus. Lumbar puncture was performed soon after her admission to hospital; the cerebrospinal fluid content of protein was 120 milligrammes per 100 millilitres, with increased globulin. The fluid was heavily blood-stained and not xanthochromic. The Wassermann test produced a negative response. The colloidal gold curve read "2222221000" and the colloidal mastic reaction read "1232110000". Electroencephalography was later performed, and the appearance suggested a space-occupying lesion in the anterior aspect of the right hemisphere. Arteriography revealed slight displacement of the anterior cerebral artery across the mid-line consistent with a deeply situated lesion in the right hemisphere. An X-ray examination of the chest revealed no abnormality, and the hæmoglobin value was 10·2 grammes per 100 millilitres; the white cell count was raised. Because of the electroencephalographic findings, burr holes were made, and needling of the right hemisphere revealed old blood, most likely the result of an old hæmorrhage. Histological examination of the tissue removed revealed no tumour cells, but numerous compound granular corpuscles.

Investigation of the patient's gynæcological history showed that for the last week she had had severe vaginal hæmorrhage with bright red blood, and prior to that had had three months' amenorrhœa; for twelve months previous to the amenorrhœa she had had a menstrual period every fourteen days. She was examined in consultation by Dr. A. S. B. Studdy, who considered her to be suffering from fibroid tumours and advised treatment at a later date.

With physiotherapy her condition improved and her mental outlook brightened. She was discharged from hospital to continue the exercises taught, but she could not walk.

### Brachio-Radiculitis.

DR. J. M. F. GRANT showed a male patient, aged thirty-one years, who on December 26, 1956, had developed pain in his left shoulder. One week later he noticed weakness of the left limb, which progressed till the arm was virtually useless. During that period he also suffered from paræsthesiæ in the finger tips. The pain gradually decreased over a period of two and a half months, but when the patient was originally examined he still required heavy sedation.

On examination of the patient, there was gross weakness of the whole of the left upper extremity, with wasting of muscles and loss of reflex activity, and also some weakness of the right shoulder girdle. A patchy type of sensory disturbance was present, but not of dermatomal distribution. In the left hand there was also some mottling, suggesting a vascular disturbance. A right-sided Horner's syndrome was also present. Otherwise clinical examination of the central nervous system revealed no abnormality. A full blood count and X-ray examinations of the chest and the cervical part of the spine revealed no abnormality.

### Spinal Meningioma.

Dr. Grant then showed a male patient, aged forty years, who had been admitted to hospital on February 14, 1957, his chief complaint being numbness and burning in the legs, of six or seven months' duration. He had undergone an appendicectomy four years earlier, and had had a duodenal ulcer ten years prior to his admission to hospital; he had suffered from malaria in New Guinea. The patient had been a motor-lorry driver and carrier previously, and had sustained no known injury to his back. He smoked 20 cigarettes a day, and was a mild drinker of alcohol (beer only); his home life was satisfactory.

His present illness had begun seven months earlier, when he had noticed overnight the onset of burning of the soles of the feet. There were no other symptoms at that time. He was told he had fallen arches, but arch supports did not give him relief. Five months later he noticed gradual progression of the burning up the legs, now associated with numbness. The condition spread to involve both legs simultaneously within two weeks. The upper level ceased at the lower part of the thorax, and included the abdomen below the umbilicus. He noticed slight differences in the feel of his clothes, though pin-prick and cotton wool were felt, but not normally. He suffered no urinary disturbance and no disturbance above the umbilicus. Some months before those symptoms he had suffered a sharp pain on bending or coughing, to the right of the spine at the level of the eighth thoracic vertebra. That pain had been present over the last eighteen months, but appeared only occasionally, and not always with bending. Over the last three weeks he had noticed increasing stiffness in the left knee, but not in the right knee. The legs were weaker than previously, and he tended to stagger at times. He did not drag his toes. He noticed "tightness" of the abdomen; he felt as if he was bloated. The lower part of the abdomen was also paræsthetic. He had suffered no pain one could describe as girdle pain.

On examination, the patient was found to be a pleasant, well-orientated, middle-aged man in a good state of nutrition. When he walked, he dragged both legs slightly. He could not move quickly. No abnormality was noted in the

cranial nerves, and the optic fundi were normal. There was no weakness or wasting in the limbs, and power and coordination were normal. The reflexes in the upper limbs were normal, the abdominal reflexes were absent, the knee jerks were equal and brisk on both sides, the ankle jerks were slightly exaggerated, the plantar reflexes were flexor on both sides, and no clonus was present. Investigation of sensation revealed an ill-defined upper border to pin-prick, rising to the tenth thoracic level on the left and the twelfth thoracic level on the right. All sensation below that level was blunted—cotton-wool, heat and cold, joint sensation, light touch—but vibration sense appeared intact. No abnormality was present above the tenth thoracic level. The impression was that a spinal cord lesion was present—either a plaque or an extramedullary tumour. No radiological abnormality was detected in the thoracic or lumbar parts of the spine. The cerebro-spinal fluid was under a pressure of 140 millimetres, and the Queckenstedt test showed free rise and fall; the protein content of the fluid was 106 milligrammes per cubic millimetre, and there were three white and seven red cells per cubic millimetre; the response to the Wassermann test was negative; the colloidal gold test produced no reaction; the globulin content of the fluid was slightly increased. The Kahn test produced a negative result.

A myelographic examination was carried out on March 14; five cubic centimetres of "Myodil" were introduced by the lumbar route, and the patient was fluoroscopically examined on the tilting table. The contrast medium flowed without obstruction or deviation up to the lower border of the second thoracic vetrebra, where it was completely arrested. Films showing the contrast at that level revealed that it had a regular border concave upwards and that the cord was slightly shifted towards the right side. The appearances suggested an extramedullary tumour, probably a meningioma, at the second thoracic level and more on the left side.

At laminectomy on March 22, a hard tumour measuring one inch by half an inch by a quarter of an inch was found on the anterior aspect of the cord at the second to third thoracic level; it was thought to be a meningioma.

### Constrictive Pericarditis.

DR. DOUGLAS STUCKEY and DR. R. G. EPPS showed a man, aged sixty-two years, who had been well until 1949, when he developed pneumonia with cough, fever and malaise, followed by a left-sided pleural effusion which was tapped. Dyspnœa was a troublesome symptom which persisted. Nine months later he developed ascites, which had been present intermittently up to the present time. In 1952 he developed peripheral œdema for the first time. In 1955 ascites and dyspnœa became more troublesome and were no longer adequately controlled by digitalis and mercurial diuretics, and in July, 1956, he was admitted to the Royal North Shore Hospital for full investigation.

Examination of the patient revealed orthopnœa and gross ascites, with a large umbilical hernia, an irregular pulse, peripheral œdema, enlarged liver and persistently raised venous pressure. Cardiac pulsations could not be felt, and the heart sounds were faint. An X-ray examination of the chest revealed considerable cardiac enlargement, with hilar congestion and small pleural effusions on both sides. Active cardiac movement was minimal, but no definite calcification was seen. An electrocardiogram revealed auricular fibrillation, low voltage in the standard leads, right bundle block and ventricular ectopic beats. A blood examination gave the following results: the hæmoglobin value was 13·5 grammes *per centum*, the white cell count was normal, and the erythrocyte sedimentation rate was 14 millimetres in one hour (normal two to four millimetres). Liver function tests gave substantially normal results. The blood urea content was 100 milligrammes per 100 millilitres. The basal metabolic rate and the blood cholesterol level were normal. Cardiac catheterization revealed a moderate increase in pressures in the right heart chambers, with a characteristic high diastolic plateau in the right ventricular tracing. There was no evidence of left to right shunt.

Operation was advised, but declined, and the patient was treated with a low salt intake, digitalis and mercurial diuretics, and with abdominal paracentesis from time to time.

### Rheumatoid Arthritis with Systemic Lupus Erythematosus.

DR. P. J. BENJAMIN showed a man, aged sixty-two years, who had been first examined on September 17, 1956. Six years previously, in mid-winter, he had begun to suffer from pains in the various joints of the upper and lower limbs, but progress was gradual and there was very little swelling until four years later, when the condition moved to the hands. Over the last six months the disease had raced ahead. He had had "Meticorten", which relieved him for a while. He had lost 14 pounds in weight. He had had no previous illness of any consequence, and there was nothing of note in his family history.

On examination of the patient, his shoulders, elbows, wrists, and metacarpo-phalangeal and interphalangeal joints were all involved on both sides. Nodules were present on the olecranon on both sides. Glands were enlarged and the spleen was normal. There were no skin manifestations. X-ray examination of the hands revealed bilateral and general demineralization of both hands. Some periarticular swelling was present, and the lesions of the hands were typical of rheumatoid arthritis. A blood examination gave the following information. The erythrocyte sedimentation rate was 50 millimetres in the first hour (Westergren); the L.E. phenomenon was demonstrated. The total serum protein content was 6·5 milligrammes per 100 millilitres (albumin 2·5, globulin 4·0 milligrammes). Paper electrophoresis gave the following result: $\alpha_1$ globulin 0·4 milligramme, $\alpha_2$ globulin 1·1 milligrammes, $\beta$ globulin 0·9 milligramme, $\gamma$ globulin 1·6 milligrammes, all per 100 millilitres.

The patient was treated with chloroquine, 200 milligrammes twice a day, and sulphadiazine, one tablet three times a day. It was also noticed in this case that the patient had clubbing of the finger nails, which had been present for a long time. An X-ray examination of the chest (Dr. B. P. Anderson Stuart) on January 30, 1957, showed a diffuse increase in the pulmonary markings on both sides, particularly at the bases. The findings suggested widespread pulmonary fibrosis, the ætiology of which was uncertain. There was no evidence of any other abnormality. Dr. Benjamin said that the patient's condition had improved, but he was still not in remission.

### Rheumatoid Arthritis with L.E. Phenomenon.

Dr. Benjamin also showed a woman, aged thirty-five years, whose right knee early in November, 1956, had became swollen and stiff, but not very painful. The fluid was removed and local injections of hydrocortisone were given; that gave relief for three days only. Stiffness developed in the shoulders, but subsequently was relieved. The left knee had become swollen two weeks prior to the meeting. At the same time the right wrist became swollen, and the right ankle was now swollen. The patient had had no previous illness of any consequence. There was no family history of chronic rheumatism.

On examination of the patient the right knee was swollen and stiff. Flexion was limited to 45°, and extension was also limited to within 5% of final extension. The left knee was swollen, but movement was only slightly restricted. The right ankle was swollen and painful on movement. The right wrist was swollen, and movement was limited in all directions; there was a large swelling the size of a hen's egg on the dorsum of the wrist extending up over the dorsum of the hand. A blood examination gave the following information. The erythrocytes numbered 4,020,000 per cubic millimetre, the hæmoglobin value was 10·9 grammes *per centum* and the colour index was 0·9. In a blood film, a few small forms of regular shape were seen, and the platelets were normal; the leucocytes numbered 6800 per cubic millimetre, 68% being neutrophile cells, 18% lymphocytes, 7% monocytes and 47% eosinophile cells. The L.E. phenomenon was demonstrated. The uric acid content of the blood was 1·6 milligrammes per 100 millilitres. The erythrocyte sedimentation rate (Westergren) was 21 millimetres in one hour. Treatment was begun with chlorquine, 200 milligrammes twice a day, and sulphadimidine, one tablet three times a day. There were no predisposing factors of stress, overwork *et cetera*. The patient had no children, and there was no other relevant history.

### Disseminated Lupus Erythematosus.

DR. R. G. ROBINSON showed a female patient, aged fifteen years, who complained of severe joint disability, pain, swelling, constitutional symptoms and a rash on her face. She had been a promising athlete, who underwent intensive training until she suffered from pleurisy in March, 1953. With treatment the condition cleared, but she failed to recover general health, and she had recurrent sore throats with cervical adenitis. In April, 1954, joint symptoms confined her to bed and then to hospital for six months; she was discharged, somewhat relieved, to rest further, and to

take 50 grains of aspirin daily. During her stay in hospital, after injection of the knees with hydrocortisone the butterfly rash on the face appeared.

On examination, she was seen to be a pale, thin girl, with many swollen, stiff, deformed joints and great muscle wasting. A butterfly rash was present on her face. The liver and spleen were enlarged, general adenitis was present, and there were nodules on each elbow; there was poor circulation in her hands and feet, which were puffy, clammy and cyanotic. A soft, blowing, systolic murmur was heard in all areas of the heart. No abnormality was detected in the chest. Laboratory investigations gave the following results. The hæmoglobin value was 13·5 grammes *per centum*. The leucocytes numbered 14,000 per cubic millimetre, 71% being neutrophile cells, 5% eosinophile cells, 1% basophile cells, 18% lymphocytes and 5% monocytes. The erythrocyte sedimentation rate was 16 millimetres in one hour. The L.E. phenomenon was demonstrated. The urine contained a few pus cells, and was sterile. A throat swab yielded a profuse growth of *Streptococcus viridans*. The serum total protein content was 7·6 grammes *per centum* (albumin 4·3 grammes, globulin 3·3 grammes). The thymol turbidity was 4·9 units, and the zinc sulphate turbidity was 6·6 units. Electrophoresis showed that the $\alpha_2$, $\beta$ and $\gamma$ globulins were increased.

The patient was treated with "Achromycin", 50 milligrammes per day, and chloroquine, 0·4 gramme per day. In one month the joints were less painful and swollen, the effusions were less, the rash was clearing, the adenitis was subsiding, the liver and spleen were not palpable, and the patient was eating and sleeping better; she had less morning stiffness, and had gained two pounds in weight. In four months the maximal constitutional improvement had been achieved. Phenylbutazone (100 milligrammes three times a day) and intraarticular injection of hydrocortisone after aspiration were added to the treatment. In eleven months, apart from joint destruction, the patient was normal. She was still having "Achromycin", chloroquine and phenylbutazone. Laboratory investigations gave the following results. The hæmoglobin value was 15·2 grammes *per centum*. The leucocytes numbered 8800 per cubic millimetre, 67% being neutrophile cells, 7% eosinophile cells, 18% lymphocytes and 8% monocytes. The erythrocyte sedimentation rate was five millimetres in one hour. The L.E. phenomenon was not demonstrated. The serum total protein content was 6·4 grammes *per centum* (albumin 3·9, globulin 2·5). The thymol turbidity was 2·8 units. The electrophoretic pattern was normal. A throat swabbing yielded a growth of *S. viridans*.

Dr. Robinson said that the case illustrated the futility of continuing to administer salicylates over long periods. The patient had taken aspirin for fourteen months and was slowly becoming a cripple. It was time that the myth about the efficacy of a bottle of aspirin or salicylates in chronic rheumatic disease was exploded. If patients did not obtain rapid and adequate relief, or if the disease was progressing, then some other form of treatment must be used. At the best aspirin was only a blocking agent, so that one could hope for a result only in a mild, self-limiting disease. In any event, symptomatic treatment could not be expected to be of much value in a disease such as that described, unless effective, active, specific treatment was carried out.

### Cavernous Hæmangioma of the Left Forearm.

DR. L. S. LOEWENTHAL showed a boy, aged sixteen years, who had been admitted to hospital in May, 1953, complaining of bilateral palmar swelling. On that occasion an hæmangioma was excised from the right palm, and his right hand had given no further trouble. Since then the swelling in the left palm had increased. The forearm had increased in size, and the left hand sweated freely. The patient had noted some numbness and weakness in the left hand. There was no history of trauma.

On examination of the patient, the right hand was normal except for a small scar. In the left forearm and hypothenar eminence was a compressible swelling. A bruit could be heard in the left antecubital fossa. The hand was hot and sweating. No abnormality was detected in a plain X-ray film of the forearm. The venous oxygen saturation in the left arm was 81% and in the right arm 33%. There was no enlargement of the heart. A phlebogram showed grossly dilated and tortuous veins, and arteriograms suggested an arterio-venous fistula.

Dr. Loewenthal said that the investigations had confirmed the presence of an arterio-venous communication. The condition was increasing and interfered with the patient's work of quarry worker. It was proposed to explore the forearm and ligate the arterio-venous fistulæ, and to excise as much hæmangiomatous tissue as possible.

### Carcinoma of the Gall-Bladder.

DR. ERIC GOULSTON showed a female patient, aged sixty-two years, suffering from carcinoma of the gall-bladder. In 1927 a cholecystostomy had been performed. In July, 1953, she had reported, complaining of epigastric pain of four months' duration. On examination of the patient, her temperature was 102° F., and a tender tumour was present below the old cholecystostomy scar. She was given antibiotics and the abscess was drained; culture produced a growth of *Bacterium coli*. A Graham's test revealed no calculi; there was no dye concentration. She was to be readmitted to hospital in two months' time for cholecystectomy. In October, 1953, a persistent sinus had formed at the point where the abscess had been incised, and cholecystectomy was performed; the gall-bladder, which was thick-walled, was removed. Convalescence was uneventful. Pathological examination of the gall-bladder showed that it bore a friable, fungating, papillary carcinoma over two-thirds of its inner wall. In November, 1953, she was admitted to hospital with a discharge from the drainage tube wound, and surrounding induration. A biopsy from the wound revealed granulation tissue, but no carcinoma cells. The discharge from the wound gradually ceased and the patient was sent home. Since that time she had attended the out-patient department regularly for check-ups.

She had been readmitted to hospital on February 2, 1957, complaining of soreness under the scar. A ventral hernia was present. On examination of the patient, a tumour was present in the abdominal wall, with keloid formation around the old scar. A large, reducible, ventral hernia was present. At operation on February 18 a large block of tissue was resected; it contained the abdominal wall tumour, surrounding skin, muscle, peritoneum, omentum and a small piece of liver. The defect in the wall was repaired with tantalum gauze, and the skin edges were pulled together. Micropathological examination revealed adenocarcinoma, the appearance resembling that of the original gall-bladder tumour. The post-operative period was complicated by thrombosis of leg veins and some breakdown of the abdominal wound.

Dr. Goulston also showed a female patient, aged fifty-eight years, who complained of attacks of pain in the right upper quadrant of the abdomen of three years' duration. The pain resembled that of biliary colic. She had been treated medically with a diet of low fat content, but as the attacks had increased in severity she sought the advice of a surgeon. A Graham's test on December 13, 1956, revealed a single opaque stone and a non-functioning gall-bladder.

On examination of the patient, she was an obese, jovial woman looking her stated age of fifty-eight years. Some tenderness was present in the right hypochondrium. No other abnormality was detected on examination, and investigations gave negative results. Operation was performed on January 23, 1957, and a chronically thickened gall-bladder containing several calculi was removed. There were adhesions to the duodenum. The common bile duct was not enlarged, and no calculi were palpated therein. She made an uninterrupted recovery, and at the time of the meeting was apparently in excellent health. The pathologist reported that the lesion was a very poorly differentiated glandular carcinoma of the gall-bladder with much surrounding inflammation.

Dr. Goulston said that although one usually associated carcinoma of the gall-bladder with jaundice and extensive secondary spread, the two patients he had shown had enjoyed several years of good health.

### Ileo-Rectal Anastomosis for Chronic Ulcerative Colitis.

DR. T. F. ROSS showed a male patient, aged forty-seven years, who had suffered from chronic ulcerative colitis with exacerbations of increasing severity for two and a half years, so that eventually he was passing blood and mucus every hour, day and night. In the year prior to examination he had lost three stone in weight. Radiographic examination revealed the typical picture of ulcerative colitis, but sigmoidoscopic examination revealed no more than granular proctitis. When the patient was examined in April, 1954, shortly before operation, he was seen to be very ill and wasted; he was constantly passing blood and mucus with very little fæcal matter every hour or so. He had severe

microcytic anæmia, which was treated by frequent blood transfusions.

It was decided to resect the colon and conserve the rectum according to the method recently described by Aylett. As his condition was so poor, it was decided to perform the operation in stages. On April 15 the first stage was performed, the abdomen being explored through a long paramedian incision. The colon was seen to be the seat of inflammatory changes throughout its length from the caecum to the upper part of the rectum. It was thickened and œdematous, which made it stiff and difficult to handle. There were numerous pericolic adhesions throughout its length. The lymph nodes were not enlarged. The terminal portion of the ileum was not affected. This was transected, and the proximal end was anastomosed end to side to the rectum as low down as possible. The distal end of the ileum was closed. The pelvic colon was then brought out through a small incision in the left iliac fossa as a loop colostomy and immediately divided, the ends being left open. The proximal end was to drain the colon, the distal to act as a safety valve for the rectum. This they did, the proximal end draining blood and mucus, and the distal end ileal contents, the latter for some days only; the patient then regained rectal function, and passed liquid fæces every hour or so.

Fourteen days later, the colon between the colectomy and the ileo-rectal anastomosis was excised; eleven days later still, the colon was excised. Adhesions made this a difficult operation. The patient recovered well, except that a small pelvic abscess had to be drained fourteen days later.

Dr. Rose said that convalescence was trying, because of the frequent passage of liquid "burning" stools, which caused intense pruritus. However, the rectum had become more accustomed to its new function, and at the time of the meeting, three years after his colectomy, the patient passed semi-solid motions three or four times a day, and rarely had to defæcate at night. He had been at his work for two years and nine months, and had gained one and half stone in weight. He ate what he liked. There was so far no evidence of rectal involvement or carcinoma, which was the main drawback of that operation, according to its opponents.

Dr. Rose then showed a female patient, aged twenty years, who had been first examined at the age of fourteen years, when she commenced to have continuous attacks of diarrhœa, passing four liquid motions containing mucus per day. In spite of treatment, that condition proceeded in seven months to become frank ulcerative colitis, with the passage of 10 to 15 stools per day, each containing much blood. After a month improvement occurred, though the patient always passed four liquid stools a day at least; however, every now and then a relapse would occur, and blood-stained stools would be passed.

When she reached the age of eighteen years (eighteen months prior to the meeting), the patient's condition became very much worse, and she passed stools consisting mainly of blood and mucus every half-hour or so, so that she lost considerable weight and was forced to stay at home from her work as a salesgirl. Sigmoidoscopic examination now revealed for the first time typical ulcerative colitis with rectal involvement. Consequently a colectomy with ileo-rectal anastomosis was performed in one stage. The patient recovered from the operation well, except for two minor attacks of small bowel obstruction, which yielded to conservative therapy.

Dr. Rose said that the patient was twenty years of age, and now, eighteen months after operation, she was a strong, healthy, well-developed young woman, whose weight was nine and a half stone. She passed four usually well-formed motions a day without blood and mucus. She had no *pruritus ani*. She was no longer nervous, and the rectum appeared to be normal. The operation had been performed because of the patient's youth, in an attempt to avoid an ileostomy, and it had so far been successful.

### Cushing's Disease.

DR. V. H. CUMBERLAND showed a female patient, aged twenty-eight years, who had been well until one year before her admission to hospital, when she noticed that her face was becoming rounder and she developed acne. Later she noticed that she was gaining in weight, but that her legs were becoming thinner. In November, 1955, she noticed hirsutism, and in January, 1956, amenorrhœa. During 1956 she had noticed increasing weakness and spontaneous bruising. There were no significant past illnesses and no significant family history.

On examination of the patient, she had features of Cushing's syndrome. Her face was round, her trunk was obese and her limbs were thin. There was generalized lanugo hair, and purple striæ were present over the thighs and the lower part of the abdomen. Her blood pressure was 180 millimetres of mercury, systolic, and 135 millimetres, diastolic, and Hess's test produced a positive result.

Investigations gave the following results. A full blood count revealed no abnormality, but there was an absence of eosinophile cells. The serum electrolyte contents, in milli-equivalents per litre, were as follows: sodium 146, potassium 3·9, chloride 102, carbon dioxide combining power 31. The blood urea content was 31 milligrammes per 100 millilitres, the 17-ketosteroid excretion was 18·9 milligrammes per day (normal, four to sixteen), and the 17-hydroxycorticoid excretion was 6·5 milligrammes per day. After four days' treatment with prednisone there was an increase in the excretion of 17-ketosteroids and 17-hydroxycorticoids. Examination of the cerebro-spinal fluid revealed no abnormality. An electroencephalogram suggested the presence of a focal cortical or subcortical abnormality over the left mid-parieto-temporal region. In view of this finding a pneumo-encephalographic examination was made; it revealed no abnormality. Excretion pyelography revealed no evidence of adrenal enlargement or any other abnormality. X-ray examination of the skull revealed no abnormality, and a skiagram of the chest revealed a minute scar in the left infraclavicular region. The patient was examined in consultation by Dr. W. G. Jasper, honorary gynæcologist; he could find no abnormalities in the pelvis and no evidence of an ovarian tumour.

In view of these findings, a diagnosis of adrenal cortical hypertrophy was made, and total bilateral adrenalectomy was performed. After operation the patient became shocked, but rapidly responded to the intravenous administration of hydrocortisone and nor-adrenaline. Three days after operation her hæmoglobin level fell to 8·6 grammes *per centum*, and occult blood was present in the fæces. She was therefore given transfusions on several occasions. Bleeding from the alimentary tract continued for fifteen days, and during this time she required multiple transfusions. A barium meal X-ray examination at that time revealed no evidence of ulcer, but the bleeding was considered due to acute ulceration from the large doses of cortisone she was having. However, as the cortisone dosage was reduced below 100 milligrammes per day bleeding ceased, and she remained well thereafter. There were no other post-operative complications. Her blood pressure before her discharge from hospital was 150 millimetres of mercury, systolic, and 100 millimetres, diastolic, and the maintenance dose of cortisone was 25 milligrammes per day. She was advised to take a diet of high protein and calcium content, and to take extra cortisone for any intercurrent infections or stress and to notify Dr. M. Leon. Microscopic examination of the adrenal gland removed at operation revealed apparently normal glands, except for some increase in the proportion of cortical to medullary tissue.

Dr. Cumberland said that the patient's present status was satisfactory, her blood pressure was normal, she had lost hair from her face, and her acne had resolved. Her menstrual periods had returned, and she had lost approximately one stone in weight, and also the feeling of weakness which had been present prior to operation.

### Linitis Plastica.

DR. N. A. FOWLER showed a male patient, aged seventy-five years, who had been operated upon some five years before his present admission to hospital, and at that operation a gastro-enterostomy had been established for a pre-pyloric ulcer. The operation was followed by a remission of dyspeptic symptoms which had been present for some years. In February, 1957, he presented at the out-patient department, complaining of increasing giddiness of twelve months' duration, of general weakness, lack of well-being and recurrent nausea of nine months' duration, and of mild epigastric pain, not related to meals, of ten weeks' duration. On his being questioned, he admitted to a loss of about one and a half stone in weight, the loss having occurred gradually over a period of about four years.

Physical examination showed the patient to be a man looking less than his age, but very pale. Abdominal examination revealed an incisional hernia in the epigastrium, through which could be felt a mobile, non-tender mass about three inches in diameter. The mass was stony hard and was of irregular contour. No other masses were palpable, but the lower edge of the liver could be felt through the hernia; the liver appeared normal in consistency

and was not attached to the palpable mass. A diagnosis of carcinoma of the pyloric antrum was made, and the patient was admitted to hospital for laparotomy—a procedure which was delayed for one week because a blood count showed his hæmoglobin value to be 36% (5·2 grammes *per centum*).

At operation a carcinoma was found extending from the edge of the previous gastro-enterostomy to the pylorus. The carcinoma was attached to the liver, part of which had to be resected, involved the whole of the circumference of the stomach, and was of the nature of *linitis plastica* (the localized form). Subtotal gastrectomy was performed after general abdominal palpation had revealed no evidence of lymphatic or hæmatogenous spread.

Dr. Fowler said that the case was presented to raise the question whether gastro-enterostomy should ever be used as a means of treatment of gastric ulcer, particularly if that ulcer was in the prepyloric region.

### Megacolon.

DR. E. LANGLEY showed a male patient, aged nineteen years, who had always had trouble with his bowels. During the last five weeks he had had attacks of epigastric pain and occasional vomiting. The pain and vomiting had been worse over the four days before his admission to hospital. He had been passing flatus but little else for some days.

On examination of the patient, his abdomen was grossly distended and his tongue was dirty. The bowel sounds were rather active, but there was no visible peristalsis. Enemata produced some flatus and fæces, but little appreciable difference. X-ray examination revealed a grossly dilated bowel and fluid levels. Sigmoidoscopic examination and the passage of a rectal tube produced considerable flatus but not complete relief, so laparotomy was performed next day. Volvulus of a very large sigmoid colon was found. The volvulus was unwound and a tube was passed into the rectum.

The patient's post-operative state was satisfactory, but further distension gradually developed, and he was prepared for resection of the sigmoid loop. Resection was performed by the Miculicz technique because of the great disparity in size. The colostomy was later closed. Unfortunately the rectal biopsy was not deep enough to show whether Meissner's and Auerbach's plexuses were present.

Dr. Langley said that the patient was of interest because of doubt about the ætiology—whether the megacolon was entirely due to chronic volvulus with obstruction, or (more probably) had a neurogenic origin (Hirchsprung's disease). Though troubled with some constipation, the patient had been well since his discharge from hospital nearly one year before.

### Carcinoma of Eyelid.

DR. DAVID DEY showed a man, aged seventy-six years, who had had a "rodent ulcer" treated by irradiation in 1946; a recurrence had developed in 1955. That and the scar left by the irradiation were excised in January, 1956, the total area being large and closed by means of a split graft from his arm. That contracted and produced an ectopion of his lower lid, which required a further post-auricular skin graft for correction. However, the size of that was relatively small, compared with the original defect. The result was pleasing, and there had been no further trouble, the full thickness graft showing no signs of contracture.

Dr. Dey also showed a man, aged sixty years, who had had a lesion in relation to his left outer canthus treated by irradiation in 1942. A recurrence one year later was treated by a radon implant. In September, 1955, a further recurrence appeared and grew rapidly. This was widely excised soon after, and the defect was filled with a forehead flap. However, the excision was inadequate in the case of the lower lid, and further recurrence became evident there in March, 1956. Pathological examination had shown the lesion to be a squamous carcinoma. A further excision was then performed, with removal of the whole lower lid; but the tumour was removed by blunt dissection from the surface of the globe. The original forehead flap was advanced into the defect. The patient had remained well since then.

Dr. Dey said that further recurrence would mean a very extensive mutilating operation, or palliative treatment, possibly with the cobalt bomb. The case illustrated the insidious nature of the process in that area, the necessity for accurate histological diagnosis, and the unsatisfactory results of late surgical treatment.

Dr. Dey's next patient was a man, aged sixty-six years, who had had a carcinoma removed from his right upper lid at the medial end in 1954. A recurrence became evident early in 1955, with extension deep to the lid. In July, 1955, Dr. Dey had excised the medial half of both lids and removed the orbital extension which had no bony fixation, covering the raw area by means of a forehead flap. Microscopic examination of the section showed the lesion to be a squamous carcinoma. It largely covered the patient's eye, and no signs of further recurrence being evident in February, 1957, a graft of preputial skin was used by Dr. K. Armstrong to restore the conjunctival fornices. The patient's progress to date was satisfactory, but he would need further surgery to his lids to improve their appearance.

The fourth patient shown by Dr. Dey was a man, who in 1955 had been diagnosed as having a rodent ulcer of the right lower lid; it was treated with irradiation. In July, 1956, he presented with a recurrence of six months' standing, involving most of the lid including the conjunctiva. In September a radical excision of the lid and adjacent part of the cheek was performed, a split skin graft was applied to the area, and a lined pocket was constructed on the forehead in preparation for replacement of the lid. All areas healed well, and there was no evidence of recurrence. Once again, microscopic examination of sections showed the lesion to be a squamous carcinoma. In February, 1957, the prepared lined flap was brought down and used to replace the lid, being divided after three weeks, and the unwanted portion returned to the scalp. The graft had "mushroomed" a little and would need some further adjustment, but essentially had given him cover for his eye, and an adequate lower fornix.

Dr. Dey finally showed a man, aged forty-eight years, who had had a basal-cell carcinoma of the right lower lid treated with diathermy in 1954. Two years later he became aware of a recurrence, and in January, 1957, it was widely excised, the area being closed by means of a post-auricular graft. So far progress had been satisfactory, and the result was cosmetically pleasing.

### Septic Bone Infarction.

DR. M. E. LAKE showed an unmarried female patient, aged thirty-seven years, who had had a femoral herniorraphy performed in August, 1955. Eleven days after operation, as the patient was dressing to go home she felt "a crack below the left knee", which was followed by pain there for ten minutes. On the following day the upper tibial area was slightly swollen. Three days later, local tenderness and swelling of the knee were present. The limb was then immobilized in plaster, and antibiotics were administered. She was discharged from hospital three weeks later, to walk with crutches. One month later, examination showed that the upper part of the left tibia was still warmer than its fellow. Because of the radiologist's suggestion of malignant change in Paget's disease, a biopsy was then performed. This showed regenerating bone, which was reminiscent in some ways of Paget's disease. Subsequent healing was normal, and the patient was bearing weight on the limb by the fourth month. She had since been observed on several occasions, and there was no disability from the lesion.

Dr. Lake said that the case was regarded as one of osteomyelitis of the upper part of the tibia, due to an infective embolism or thrombosis of the upper tibial nutrient vessels.

Dr. Lake also showed a man, aged twenty-seven years, who had been admitted to hospital in September, 1955, for an elective gastrectomy of the Pólya type with retrocolic anastomosis. Six days after operation he complained of pain in the right lower extremity, for which infra-red therapy was ordered. He was discharged on the tenth post-operative day. The pain persisted, and at the country centre where he resided he was treated with an intensive course of antibiotics for what appeared to be acute osteomyelitis of the right femur. He was readmitted to the Royal North Shore Hospital in February, 1956. There was considerable wasting of the thigh, and the patient himself had lost two and a half stone. The diagnosis of chronic osteomyelitis was confirmed radiologically, and sequestrum formation was noted. He was discharged from hospital, to return for sequestrectomy when it was radiologically apparent that the sequestrum had separated. The operation was performed in November, 1956, and the patient's convalescence was uneventful. At the time of the meeting healing was complete and function was normal.

Dr. Lake commented that both the patients had a remarkable feature in common—the occurrence of acute osteomyelitis of a long bone within a fortnight of a major operation. There was a good deal of anatomical and pathological evidence to support the conception of those cases as

a type of septic bone infarction. That was only another way of describing the sequence of events in many cases of acute osteomyelitis. However, it was considered in the two cases under discussion that the source of infection and vascular occlusion was the preceding operation.

### Pulmonary Embolus.

DR. A. G. MCMANIS showed a married woman, aged fifty-three years, who had been known to have a "bad heart" since she was a young girl. However, it had not given her much trouble over the years. In December, 1956, she had become ill with pain in the right side of her chest. She consulted her doctor, who found signs of a pleural effusion on the right side of her chest. When that was aspirated, it proved to be blood-stained fluid. When the patient was examined in hospital, there were still signs of a pleural effusion. In addition there were signs of mitral stenosis, and auricular fibrillation was present. It was considered that the patient had had a pulmonary embolus, which had caused the pleural effusion. Dr. McManis said that the effusion did not clear; but that in itself did not cast doubt on the diagnosis, as effusions after emboli could sometimes be persistent. However, the patient's general condition deteriorated. Among further investigations, cardiac catheterization was performed; the catheter could not enter the pulmonary artery. That was taken to mean that the artery was blocked by an embolus. The patient next developed a pericardial effusion. A bronchoscopic examination revealed a partial obstruction in the left stem bronchus. There was a protrusion from the postero-lateral wall. The appearance was that of something pressing into the bronchus from without. The mucous membrane over it was quite smooth. Examination of a biopsy specimen from that region revealed normal bronchial mucosa. A scalene node biopsy was then performed, and showed evidence of an adeno-carcinoma. However, no statement could be made as to the actual site of its origin.

### Constrictive Pericarditis.

DR. IAN MONK showed a male patient, aged twenty-nine years, who at the age of sixteen years had noted swelling of the ankles and shortness of breath. Medical examination at that time revealed hepatic enlargement and ascites. Pleural effusion was also noted. He rested for several years and was able to start work at the age of nineteen years. For nearly ten years, up until a few months before his admission to hospital in September, 1956, he was able to work, although he was breathless on exertion and noted swelling of the legs on many occasions, particularly when he suffered from a respiratory infection. A few months prior to his admission to hospital he contracted a severe cold, and œdema of the legs, sacrum and abdomen was noted. Ascites and hepatic enlargement were also observed. A diagnosis of constrictive pericarditis was made by his medical attendant at Katoomba, and an X-ray examination of the chest revealed calcification of the pericardium.

On the patient's admission to hospital, physical examination revealed a slightly dusky appearance of the face, slight œdema of the legs, slight ascites, a palpable and pulsating liver, and slightly raised jugular venous pressure. Precordial diastolic pulsation was noted, the heart sounds were well heard, and a third heart sound was present. Fluoroscopic examination revealed considerable calcification, and a good pulsation of the left heart border.

On October 3 operation was performed, access to the heart being obtained by a median sternotomy from below upwards and extended on each side into the first intercostal space. The left border of the heart posterior to the phrenic nerve was cleared, then the base. The anterior surface was then cleared, and most of the left auricle. Great care was taken to clear the right side including most of the right auricle. The superior *vena cava* and the entrance of the inferior *vena cava* into the auricle were cleared completely. Complete freeing of the inferior *vena cava* could not be effected, as a calcified plaque was embedded in the wall at the junction of the inferior *vena cava* and auricle posteriorly. During an attempt to free this area the auricle was opened, and this required suturing to control bleeding. The mediastinum was drained for twenty-four hours after operation, and convalescence was uneventful. Some œdema of the legs was noted for some weeks after the patient was mobilized, but had since disappeared. A few days after operation the patient spontaneously remarked on the subjective improvement in his peripheral circulation and a feeling of "clearing" in the head—presumably due to the lowering of venous pressure. The tissue removed at operation proved to be tuberculous, despite a negative response to the Mantoux test.

# Public Health.

## THE INFLUENZA EPIDEMIC IN THE FAR EAST.

THE current influenza epidemic in the Far East has received world-wide and sometimes alarmist newspaper publicity. No account of the Hong Kong epidemic, from which the Malayan one presumably derived, has yet appeared in any of the medical journals to reach us. The following outline of the main aspects of the epidemic in the Federation of Malaya is therefore presented for the information of the medical profession in countries to which it may spread.

Influenza was made a notifiable disease in the Federation on May 4, 1957, as soon as news of the epidemic in Singapore was received. The first notification in Kuala Lumpur was on May 6, and virus isolated from this patient was dispatched, after preliminary identification, to London and Washington on May 17. Although there are various defects in the figures, the notifications demonstrate the main features of the spread of the disease. By May 10 notifications were being received from most of the large towns; but the rural areas were not widely affected until about two weeks later, and in many the peak is only now being reached. In each town the incidence has risen sharply during the first four or five days and has then been maintained for about three weeks. The spread in town and country is illustrated in Table I, which shows the notifications in the Perak North District; this contains one large town, Taiping, and a heavily populated rural area.

In Kuala Lumpur, the majority of patients early in the epidemic were poorer people living in the most crowded and least healthy environments. Since then the disease has progressively affected those living in better circumstances, so that in the fourth and fifth weeks of the epidemic more and more patients from the upper class of Asians and among the Europeans have been seen. Asian military units have so far been much more heavily affected than the British, although in one small mixed unit the difference in rate was not marked. The apparent racial difference in incidence seems therefore more likely to be due to differences in degree of exposure and general environment and health than to immunity; influenza, after all, is not uncommon in Malaya, and A prime virus was isolated during an outbreak around Kuala Lumpur as recently as 1953.

The clinical severity of the disease has varied widely, but a typical attack has the following course. Especially in children, the first complaint is usually of thirst, followed in six to twelve hours by a very sore throat. On examination, a bright red velvety inflammation is characteristically confined to the posterior pharyngeal wall. About this time the temperature is around 102° F. and the pulse about 120 per minute. A generalized headache develops three to six hours later, and in adults and adolescents is often accompanied by aching, particularly in the lower chest and lower back. Aches are uncommon in children, whose main discomforts are the sore throat and a "floating", "bloated" headache. Tonsillar enlargement without suppuration may occur during the next twenty-four hours, usually in patients with chronic tonsillitis. Dry cough is common at this stage, but no crepitations have been detected in the lungs of uncomplicated cases. By the third day the cough is brassy and associated with tracheitis. During the second twenty-four hours, the fever is maintained but the sore throat disappears, and the headache and muscular aches diminish. Recovery is usual by the fourth day, and most patients return to work after about five days' absence. Vomiting has not been marked except in those intolerant of salicylates or given solid food during the first twenty-four hours.

Although the incidence of influenza has been very high, the number of deaths attributable to it has been very small. Most patients have been able to go to clinics for treatment, but some have been too weak to stand—about 10% in a children's clinic—and several fainted while awaiting treatment. Several young children have shown meningism, and this has been noted in three fatal cases[1] which had terminal convulsions and coma. These cases were not proven virologically.

About 10% of patients return to the clinic after the third or fourth day with secondary bronchitis, tonsillitis, *etc.* A few patients have had a short recurrence of fever about the seventh or eighth day.

[1] Reported by Dr. Saraswathy, General Hospital, Kuala Lumpur.

TABLE I.

*Notifications of Influenza in Perak North District of Malaya.*[1]

| Location. | Estimated Population, 1957. | Dates: May, 1957. | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 | 31 |
| Urban | 60,000 | 41 | 23 | 35[2] | 83 | 335 | 310 | 488 | 665 | 351 | 295[2] | 869 | 861 | 771 | 663 | 603 | 604 | 144[2] | 646 | 528 | 551 | 423 | 304 |
| Rural | 230,000 | | 22 | | | 10 | 39 | 66 | 76 | | 42[2] | 73 | 59 | 222 | 341 | 76 | 158 | 37[2] | 274 | 269 | 251 | 287 | 110 |

[1] We are greatly indebted to Dr. S. P. Maurer, Health Officer, Perak North, for the careful daily records of notifications.

[2] Sundays.

Symptomatic treatment with salicylates has been very effective when combined with strict bed-rest for two or three days, a bland diet, and copious fluids. Intramuscular chloramphenicol has been given in a number of severe cases with apparent benefit, but controlled evaluation of this observation has not been possible.

Several strains of virus have been isolated in this Institute by us and by the United States Army Medical Research Unit working here; four of them have so far been sent to the World Influenza Centres in London and Washington for detailed study. Hæmagglutinin-inhibition tests with the first three strains isolated at once showed that they were unrelated to strains for which antisera were available to us (*i.e.*, A: PR8; A prime: FM-1, FW/1/50, FLW/1/52; B: LEE, IB-1, B/Malaya/5/55). Subsequently, A/Nederlands/56 antiserum and virus were received from Dr. C. H. Andrewes (World Influenza Centre, London), and our new isolates were shown to be unrelated to it. A complement-fixation test with a representative strain has shown that the new isolates belong to type A. Paired sera (acute and convalescent phases) of patients from several parts of the Federation were tested by hæmagglutinin-inhibition against the newly isolated strains and against the reference strains listed above, and significant rises in the antibody titre were found only against the new strains.

C. E. GORDON SMITH, M.D.,
L. H. TURNER, M.D. (Institute for Medical Research, Kuala Lumpur),
C. J. V. HELLIWELL, M.B., B.S. (General Practitioner, Kuala Lumpur).

June 4, 1957.

## Out of the Past.

*In this column will be published from time to time extracts, taken from medical journals, newspapers, official and historical records, diaries and so on, dealing with events connected with the early medical history of Australia.*

### THE NEW SOUTH WALES MEDICAL GAZETTE.[1]

THE projectors of this Journal in common with many members of the medical profession have long felt the want of some recognized organ by which, and through which, the accumulated results of individual experiences might be communicated to the general body. The columns of the daily press—even were they always open to us—are not the proper places for the discussion of medical and surgical questions, and although it has often been said "we ought to have a Medical Journal" the matter always rested there—no one seemed inclined to take it up. The Medical Officers of the Volunteer Force being to a certain extent an organized body and in the habit of meeting occasionally for the consideration of such matters as more particularly interested them, considered this question amongst others, and finding that there was otherwise no probability of anyone else attempting to establish what was acknowledged to be a desideratum, they resolved, though with considerable diffidence and hesitation, to set their own shoulders to the wheel, and the result is the present number. In thus taking the initiative in the establishment of such a periodical we do not desire to arrogate to ourselves as a body, any position superior to that of the other members of the profession. On the other hand we are willing to admit that there may be found others better qualified, in every respect, to conduct such an undertaking: but we have taken the task upon ourselves purely and simply because—the want being recognized—no one else would do it and we therefore hope to receive our meed of encouragement and sympathy.

October, 1870.

[1] From the original in the Mitchell Library, Sydney.

## Correspondence.

### THE NEW SOUTH WALES MEDICAL REGISTER.

SIR: *Re* annual roll fee, 1958. Reminders have been sent to all practitioners informing them that the annual roll fee of £1 1s. (*plus* exchange on country cheques) is due for payment by June 30, 1957.

The importance of maintaining currency of registration cannot be over-emphasized. If, owing to change of address or other circumstances, no reminder has been received, it is requested that payment be made direct to the Board.

Yours, etc.,

P. E. COSGRAVE,
Secretary.

New South Wales Medical Board,
Winchcombe House,
52 Bridge Street,
Sydney.
June 3, 1957.

### THE GOOD LIFE.

SIR: "The habit of well directed mind" is discussed in the leader of the journal of June 1, 1957. This directs us to Osler's "A Way of Life", and it is from this we may learn "something of 'the good life' ". Those of our profession who were bred before the turn of the nineteenth century into the twentieth, not only came to revere Osler, but became familiar with his life, described particularly by Cushing.[1] But they of a later generation may, perhaps, not know what is the main prescription in that lay sermon, preached to the students of Yale on a Sunday in 1913. In "A Way of Life" Osler tells: "Begin the day with Christ and His Prayer—you need no other. Creedless, with it you have religion; creed-stuffed, it will leaven any theological dough in which you stick." Cushing also tells us that Osler inscribed the following poem, "The Salutation of the Dawn", rendered[2] from Sanskrit, and noted on a reprint of that address kept in his library:

Listen to the Exhortation of the Dawn!
Look to this Day!
For it is Life, the very Life of Life.
In its brief course lie all the
Varieties and Realities of your Existence:
The Bliss of Growth,
The Glory of Action,
The Splendour of Beauty;
For Yesterday is but a Dream
And Tomorrow only a Vision;
But To-day well lived makes
Every Yesterday a Dream of Happiness,
And every Tomorrow a Vision of Hope.
Look well therefore to this Day!
Such is the Salutation of the Dawn!

[1] "The Life of Sir William Osler", by Harvey Cushing, Oxford University Press, London. Complete in one volume, 1940.

[2] Frontispiece of "Words in Pain", anonymous, G. M. Bishop, London, 1919.

(by whom? sent me 26.vi.18 by de Havilland Hall to whom they were given by a remarkable woman, Mrs. Jacoby. If another reprint is called for put this on this page. Wm. Osler.)

Yours, etc.,

Burleigh Heads, Queensland, June 4, 1957.

NORMAN MARKWELL.

# Post-Graduate Work.

## THE POST-GRADUATE COMMITTEE IN MEDICINE IN THE UNIVERSITY OF SYDNEY.

### Week-End Course in Pædiatrics.

THE Post-Graduate Committee in Medicine in the University of Sydney announces that a week-end course in pædiatrics will be held in the Doreen Dew Theatre (new Lecture Theatre and Conference Room) of the Royal Alexandra Hospital for Children, Bridge Road, Camperdown, on Saturday and Sunday, August 3 and 4, 1957, under the supervision of Professor Lorimer Dods. It is hoped that it may be possible to arrange for members to observe certain minor technical problems in the wards during the course, the programme of which is as follows:

Saturday, August 3: 9.30 a.m., "Medical Emergencies and Other Problems of the Newborn Period", Dr. S. E. L. Stening; 11 a.m., "Common Urological Problems of Infants and Children in General Practice", Dr. E. S. Stuckey; 12 noon, "The Management of Acute and Recurrent Bronchitis during Infancy and Childhood", Dr. J. Beveridge; 2.15 p.m., "Some Aspects of Preventive Pædiatrics", Professor Lorimer Dods; 3.45 p.m., "Common Therapeutic Problems of Pædiatric Practice", Dr. A. Tink.

Sunday, August 4: 9.30 a.m., "Intrathoracic Surgery of Infancy and Childhood in Relation to General Practice", Dr. Douglas H. Cohen; 11 a.m., "Lead and Other Forms of Poisoning during Infancy and Childhood", Dr. D. Kerr Grant; 12 noon, "Minor Technical Procedures", Dr. J. Harley; 2 p.m., "The Practical Approach to Various Minor Pædiatric Problems", Dr. S. E. J. Robertson; 3.30 p.m., question time, Dr. M. Sofer Schreiber and Dr. S. E. J. Robertson.

The closing date for applications is July 26, 1957, and the fee for attendance, including luncheon, is £4 16s. The fee for members who do not require luncheon is £4 4s. Early written applications, enclosing remittance, should be made to the Course Secretary, Post-Graduate Committee in Medicine, 131 Macquarie Street, Sydney. Telephones: BU 4497-8. Telegraphic address: "Postgrad Sydney."

### Clinical Meetings at Balmoral Naval Hospital.

The Post-Graduate Committee in Medicine in the University of Sydney announces the following programme of monthly clinical meetings to be held at the Balmoral Naval Hospital from August to December, 1957, beginning at 2 p.m.: Tuesday, August 13, "Common Skin Diseases and Their Treatment", Dr. A. Geoffrey Finley; Tuesday, September 10, "Recent Advances Abroad", Dr. K. J. Fagan; Tuesday, October 8, "Impressions of Medical Advances Overseas", Dr. Selwyn Nelson; Tuesday, November 19, "Treatment of Eye Conditions Encountered in Service Personnel", Dr. E. W. Freshney; Tuesday, December 10, "Psychosomatic Diseases", Dr. T. M. Greenaway.

All members of the medical profession and senior medical students are invited to attend.

### Post-Graduate Residencies for Women Medical Graduates.

The Post-Graduate Committee in Medicine in the University of Sydney announces that post-graduate residencies for women medical graduates will be available from time to time at the Rachel Forster Hospital for Women and Children, Pitt Street, Redfern, for periods from one to two weeks, or longer by arrangement. Intending applicants should apply as early as possible, stating the period of resident training required and any special interests. The fee for attendance is £6 6s. per week. Application should be

## DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED JUNE 8, 1957.[1]

| Disease. | New South Wales. | Victoria. | Queensland. | South Australia. | Western Australia. | Tasmania. | Northern Territory. | Australian Capital Territory. | Australia. |
|---|---|---|---|---|---|---|---|---|---|
| Acute Rheumatism | 1 | 7(6) | 4(2) | .. | .. | .. | .. | .. | 12 |
| Amœbiasis | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Ancylostomiasis | .. | .. | 1 | .. | .. | .. | .. | .. | 1 |
| Anthrax | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Bilharzias | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Brucellosis | .. | 1(1) | .. | .. | .. | .. | .. | .. | 1 |
| Cholera | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Chorea (St. Vitus) | .. | 1(1) | .. | .. | .. | .. | .. | .. | 1 |
| Dengue | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Diarrhœa (Infantile) | 1(1) | 9(8) | .. | .. | .. | .. | 3 | .. | 13 |
| Diphtheria | 1 | .. | .. | .. | 2(2) | .. | .. | .. | 3 |
| Dysentery (Bacillary) | .. | 1(1) | 2(1) | 1(1) | .. | .. | .. | .. | 4 |
| Encephalitis | 1(1) | 1(1) | .. | .. | .. | .. | .. | .. | 2 |
| Filariasis | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Homologous Serum Jaundice | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Hydatid | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Infective Hepatitis | 49(18) | 26(11) | .. | 3(2) | 6(5) | 1 | 1 | 1 | 87 |
| Lead Poisoning | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Leprosy | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Leptospirosis | 4 | .. | 2 | .. | .. | .. | .. | .. | 6 |
| Malaria | .. | .. | 1(1) | .. | .. | .. | 9 | .. | 10 |
| Meningococcal Infection | 4(1) | 2 | 2 | .. | .. | 1 | .. | .. | 9 |
| Ophthalmia | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Ornithosis | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Paratyphoid | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Plague | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Poliomyelitis | 1(1) | .. | .. | .. | .. | .. | .. | .. | 1 |
| Puerperal Fever | 2(1) | .. | .. | .. | .. | .. | .. | .. | 2 |
| Rubella | .. | 31(24) | .. | 17(6) | 2(2) | .. | .. | .. | 50 |
| Salmonella Infection | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Scarlet Fever | 13(7) | 36(23) | 2(2) | 4(2) | 5(2) | .. | .. | .. | 60 |
| Smallpox | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Tetanus | .. | 1(1) | .. | .. | .. | .. | .. | .. | 1 |
| Trachoma | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Trichinosis | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Tuberculosis | 43(29) | 20(15) | 9(3) | 4(3) | 5(4) | .. | 2 | .. | 83 |
| Typhoid Fever | .. | .. | 3(3) | .. | 1(1) | .. | .. | .. | 4 |
| Typhus (Flea-, Mite- and Tick-borne) | .. | 4 | .. | .. | .. | .. | .. | .. | 4 |
| Typhus (Louse-borne) | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Yellow Fever | .. | .. | .. | .. | .. | .. | .. | .. | .. |

[1] Figures in parentheses are those for the metropolitan area.

made direct to the Course Secretary, The Post-Graduate Committee in Medicine, 131 Macquarie Street, Sydney. Telephones: BU 4497-8. Telegraphic address: "Postgrad Sydney."

## Australian Medical Board Proceedings.

### QUEENSLAND.

THE following have been granted limited registration as medical practitioners, pursuant to Section 20 (3) of *The Medical Acts*, 1939 to 1955, of Queensland: Waugh, Shirley Lillian, M.B., B.S., 1956 (Univ. Queensland); Moser, Rudi, M.D., 1924 (Univ. Berlin).

The following have been registered, pursuant to the provisions of Section 19 (1) (*a*) and (*c*) of *The Medical Acts*, 1939 to 1955, of Queensland, as duly qualified medical practitioners: Charchalis, Jim, M.B., B.S., 1956 (Univ. Queensland); Fitzgerald, Charles Paul, M.B., B.S., 1955 (Univ. Queensland); O'Callaghan, Eugene Desmond, M.B., B.S., 1955 (Univ. Queensland); Tung, Henry Siew Yoon, M.B., B.S., 1955 (Univ. Melbourne); Trenerry, Frederick Martyn, M.B., B.S., 1956 (Univ. Queensland).

The following have been registered, pursuant to the provisions of Section 19 (1) (*a*) and (*d*) of *The Medical Acts*, 1939 to 1955, of Queensland, as duly qualified medical practitioners: Macrae, Ronald Duncan, M.B., Ch.B., 1929, D.P.H., 1931 (Univ. Aberdeen), F.R.C.S., Edinburgh, 1939; Standeven, Betty, M.B., Ch.B., 1953 (Univ. Leeds), D.R.C.O.G., 1956.

The following has been registered, pursuant to the provisions of Sections 19 (1) (*b*) and (*d*) and 19 (2) of *The Medical Acts*, 1939 to 1955, of Queensland, as a duly qualified medical practitioner: Berkowicz, Lejba, Doctor of Medicine and Surgery, 1947 (Univ. Milan).

The following additional qualifications have been registered: Lahz, John Lister Colless, F.R.C.S., England, 1954; Gregg, Ronald Francis, F.R.C.S., Edinburgh, 1957.

### TASMANIA.

THE following have been registered, pursuant to the provisions of the *Medical Act*, 1918, of Tasmania, as duly qualified medical practitioners: Thomson, Thomas, M.B., Ch.B., 1946 (Univ. Glasgow), F.F.A.R.C.S., 1956, D.A. (R.C.P. & S., England), 1954; Godlee, Theodore, M.B., B.S., 1932 (Univ. Adelaide); Wallace, Hilary Kathleen Cranleigh, M.B., B.S., 1955 (Univ. London), D.O.R.C.O.G., 1956; Wallace, Alan Galbraith, M.B., B.Ch., 1950 (Cantab.), M.R.C.P. (Edinburgh), 1955, D.O.R.C.O.G., 1954, D.C.H., 1954; Perkins, Michael Vivian, M.B., B.S., 1954 (Univ. London).

## Corrigendum.

IN the issue of June 8, 1957, at page 814, in the announcement under the heading "Faculty of Radiologists of Great Britain", the name of Dr. K. S. Mowatt appears incorrectly as "Dr. K. S. Howatt". We regret this error.

## Nominations and Elections.

THE undermentioned have been elected members of the New South Wales Branch of the British Medical Association: Breslin, Francis Hugh Dominic, M.B., B.S., 1955 (Univ. Sydney); Grahem, Owen Aubrey, M.B., B.S., 1957 (Univ. Sydney); Mason, Richard Merritt, M.B., B.S., 1956 (Univ. Sydney); Prime, Thomas Trenfield, M.B., B.S., 1957 (Univ. Melbourne); Woodhouse, Marie Alison, M.B., B.S., 1957 (Univ. Sydney); Tinsley, Richard William, M.B., B.S., 1956 (Univ. Sydney); Sharrock, Keith Douglas, M.B., B.S., 1954 (Univ. Sydney); McJannett, Alan Hugh Dalton, M.B., B.S., 1947 (Univ. Sydney); Varo, Gisela, licensed under Section 21 (*b*) of the *Medical Practitioners Act*, 1938-1957: Goldberg, Aron, regional registration for practice in the Kenny Knob, Snowy Mountains, region.

## Honours.

### CORRIGENDUM.

IN the list of Birthday Honours published in the issue of June 22, 1957, it was wrongly stated that Dr. Benjamin Thomas Edye had been created an Officer of the Most Excellent Order of the British Empire. In fact Dr. Edye has been made a Commander of the Most Excellent Order of the British Empire. We express our regret to Dr. Edye for this error.

## Deaths.

THE following deaths have been announced:

JAMES.—Geoffey Alfred James, on May 26, at South Perth, Western Australia.

HUGHES.—David Alfred Hughes, on June 15, 1957, at Sydney.

SKYRING.—Doris Una Skyring, on June 17, at Rockhampton, Queensland.

## Diary for the Month.

JULY 2.—New South Wales Branch, B.M.A.: Council Quarterly.
JULY 3.—Western Australian Branch, B.M.A.: Branch Council.
JULY 3.—Victorian Branch, B.M.A.: Branch Meeting.
JULY 5.—Queensland Branch, B.M.A.: General Meeting.
JULY 9.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
JULY 9.—New South Wales Branch, B.M.A.: Organization and Science Committee.

## Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

*New South Wales Branch* (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

*Queensland Branch* (Honorary Secretary, B.M.A. House, 88 L'Estrange Terrace, Kelvin Grove, Brisbane): Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

*South Australian Branch* (Honorary Secretary, 80 Brougham Place, North Adelaide): All contract practice appointments in South Australia.

## Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2-3.)

Members and subscribers are requested to notify the Manager, THE MEDICAL JOURNAL OF AUSTRALIA, Seamer Street, Glebe, New South Wales, without delay, of any irregularity in the delivery of this journal. The management cannot accept any responsibility or recognize any claim arising out of non-receipt of journals unless such notification is received within one month.

SUBSCRIPTION RATES.—Medical students and others not receiving THE MEDICAL JOURNAL OF AUSTRALIA in virtue of membership of the Branches of the British Medical Association in the Commonwealth can become subscribers to the journal by applying to the Manager or through the usual agents and booksellers. Subscriptions can commence at the beginning of any quarter and are renewable on December 31. The rate is £5 *per annum* within Australia and the British Commonwealth of Nations, and £6 *per annum* within America and foreign countries, payable in advance.

LICATE

UNIVERSITY OF MICHIGAN
MEDICAL LIBRARY

PUBLISHED WEEKLY

PRICE TWO SHILLINGS
AND SIXPENCE

# THE MEDICAL JOURNAL OF AUSTRALIA

VOL. I.—44TH YEAR SYDNEY, SATURDAY, JUNE 29, 1957 No. 26

COMMONWEALTH OF AUSTRALIA

*DEPARTMENT OF HEALTH*

## HÆMAGGLUTININ ALUMINIUM PHOSPHATE ADSORBED

**(H.A.P.A.)**

### Pertussis Prophylactic

This product is a specially prepared extract of virulent pertussis organisms, adsorbed on a mineral carrier; it is stable and accurately standardised for potency.

Immunization with H.A.P.A. may be commenced at the age of three months and requires only two injections instead of the usual three or four required for other pertussis prophylactics.

H.A.P.A. is issued in ampoules containing 0·5 c.c. and 5 c.c., and may be obtained from chemists and from all offices of the Commonwealth Department of Health throughout Australia, or direct from—

## COMMONWEALTH SERUM LABORATORIES

**Parkville, N.2, Victoria, Australia**

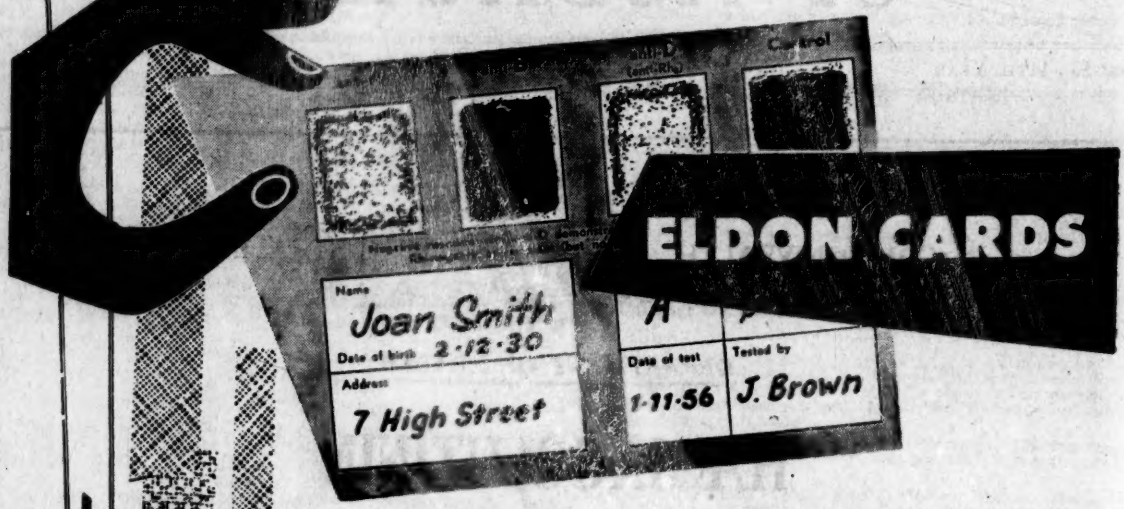
SL.100

Registered at the G.P.O., Sydney, for transmission by post as a newspaper.

an accurate and

reliable method of both ABO-Rho

and CDE blood typing




Eldon cards are coated with a cellulose film upon which especially prepared serum reagents are dried, allowing rapid grouping at room temperature. Each card carries patient's name, excluding any margin of error. The Eldon method is very simple and convenient for blood banks, hospitals and physicians.

*Manufactured by:*
NORDISK INSULINLABORATORIUM IN DENMARK

*Literature and information on request from:*

**Andrews Laboratories Pty. Ltd.**

15 HAMILTON STREET, SYDNEY

*SOLE DISTRIBUTORS IN AUSTRALIA*

Branches at:
217 North Terrace, Adelaide.
396 Flinders Lane, Melbourne.
61 Stirling Street, Perth.
309 Queen Street, Brisbane.
Bank Corner, Newcastle West.

AL.74.FT

WANDER TB PRODUCTS

*Introducing*

# "SACHETS"
# B—PAS

## a new presentation of

## B-PAS WANDER

The benzoyl derivative of PAS—B-PAS Wander—is now accepted as a better tolerated derivative of PAS in the treatment of tuberculosis. The SACHET, containing 3·5 g. B-PAS powder in a hermetically sealed plastic envelope, now provides an alternative to the well-known Cachet.

**The contents of the SACHET stirred into water or milk provide easy administration at less frequent intervals.**

**B-PAS WANDER SACHETS are available as follows: Containers of 150 × 3·5 g.; Cachets: Boxes of 400 × 1 g.**

**PHARMEDICA PTY. LTD.** "PHARMED" **KINGSGROVE, N.S.W.**

*Sole distributors for* A. WANDER LTD., Devonport, Tasmania. *Australian Division of* A. WANDER LIMITED, 42 Upper Grosvenor Street, Grosvenor Square, London, W.1.

W.9

# THE DAWN O

SYNERGISTICALLY ENHANCED
POTENCY

SIGNIFICANTLY IMPROVED
TOLERABILITY

# SYNE

TRUE BROAD E

**Dosage:** The usual adult dose is 1 to 2 capsules four times daily (1 . For

**Supply:** Synermycin is currently available in 250 mg. capsules, each of te

*Sole Distributors:*
F. H. FAULDING & CO. LTD.
Adelaide, Sydney, Melbourne, Perth, Brisbane

mark

## ...W ANTIBIOTIC ERA

OVERCOMES PATHOGENS RESISTANT TO OTHER ANTIBIOTICS

FORESTALLS EMERGENCE OF RESISTANT ORGANISMS

WIDER MARGIN OF SAFETY

# ...YCIN*

Oleandomycin Tetracycline

...E SYNERGISM

...y (1... . For children, dosage is proportionately less according to age and weight.

...each ... of tetracycline and 83 mg. of oleandomycin. Bottles of 16 and 100.

Pfizer PFIZER PTY. LIMITED, BOX 4016, G.P.O., SYDNEY

*...mark of Chas. Pfizer & Co. Inc.

# Intramuscular Iron

*and the*

# Anaemias of Infancy

**The value of Imferon in Nutritional Anaemia of Infancy and in the prophylaxis and treatment of Anaemia of Prematurity has recently been convincingly demonstrated.**

• "There was obvious rapid clinical improvement in all cases as shown by the return of appetite, change of disposition, improvement in colour, and gain in weight."

• "The daily rise in haemoglobin during the first two weeks after treatment was almost 1.5%." — *Brit. Med. J.*, 1955, 2 700.

Imferon is a practical and effective means of administering iron to infants who do not make progress on oral preparations. The increase in haemoglobin concentration is about 20% in two weeks — more than can be achieved with any form of oral therapy.

THE INDICATIONS FOR IMFERON IN INFANCY ARE:

1 Nutritional anaemia in infants who do not make progress on oral iron.
2 Nutritional anaemia in infants whose home conditions are poor and who would otherwise have to be admitted to hospital.
3 The prophylaxis and treatment of anaemia of prematurity.
4 As an alternative in some cases to blood transfusion.

*FURTHER INFORMATION IS AVAILABLE ON REQUEST TO*
*FISONS CHEMICALS (PTY.) LIMITED*
*DAKING HOUSE, 499 PITT STREET, SYDNEY PHONE: MA 4291*

Imferon is issued in ampoules of 2ml. (100 mg.Fe) in boxes of 10 and 100.

# Imferon REGD.

IRON-DEXTRAN COMPLEX

A PRODUCT OF BENGER LABORATORIES

BENGER LABORATORIES LIMITED • HOLMES CHAPEL • CHESHIRE • ENGLAND

# specific against coccic infections

Specific—because you can actually pinpoint the therapy for coccic infections. That's because you know most bacterial respiratory infections are caused by staph-, strep- and pneumococci. And these are the very organisms most sensitive to ERYTHROCIN—even in many cases when they resist penicillin and other antibiotics.

filmtab

**Erythrocin®**
(Erythromycin Stearate, Abbott)
STEARATE

# with little risk of serious side effects

Low toxicity—because ERYTHROCIN (in contrast to many other antibiotics) rarely alters intestinal flora. Thus, patients seldom get gastroenteral side effects. Or loss of vitamin synthesis in the intestine. Virtually no allergic reactions, either. *Filmtab* ERYTHROCIN Stearate (100 and 250 mg.), bottles of 25 and 100. Abbott

filmtab

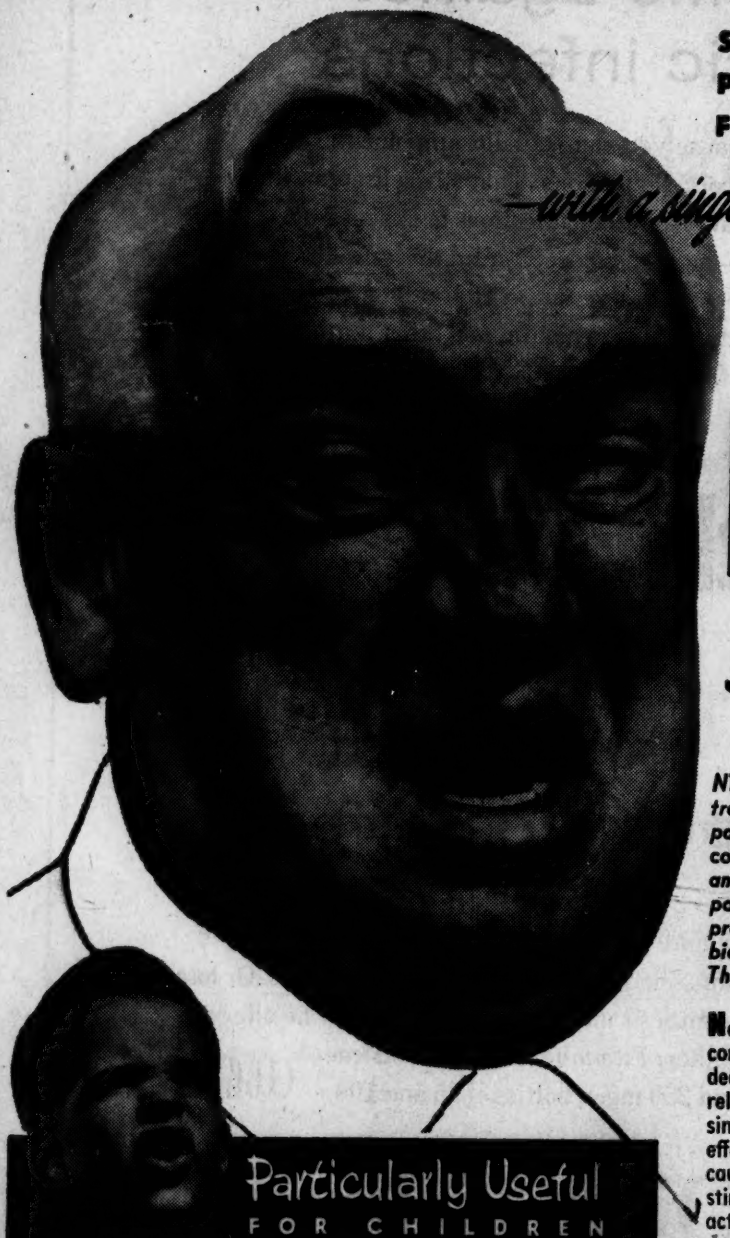
**Erythrocin®**
(Erythromycin Stearate, Abbott)
STEARATE

●Filmtab — film-sealed tablets; pat. applied for.

# DISPEL THE SYMPTOMS OF NASAL ALLERGY . . .

**SURELY,**
**PROMPTLY and**
**FOR PROLONGED PERIODS**

*—with a single synergistic preparation*



# NTz

## Spray or Drops

***NTZ** represents a more efficient means of treating congested, irritated, allergic nasal passages. This synergistic preparation combines well-established decongestant, anti-allergic and wetting agents, which potentiate one another to assure prompt and prolonged relief. NTZ contains no antibiotics which could cause sensitivity reaction. This effective formulation comprises:*

**Neo-Synephrine 0.5%**—well tolerated vasoconstrictor producing prompt and prolonged decongestion—opens the nasal passages, relieves engorged tissues and encourages sinus drainage. Neo-Synephrine is equally effective on repeated application; does not cause congestive rebound or central nervous stimulation; does not interfere with ciliary activity.

**Thenfadil 0.1%**—potent, well tolerated antihistaminic; blocks the reaction of nasal tissues to allergens and vasomotor imbalance.

**Zalkon 1:5000**—antiseptic preservative and excellent wetting agent. Promotes penetration to less accessible nasal areas.

## Particularly Useful FOR CHILDREN

Of a squeeze-type container Silbert[1] remarks: *"It is particularly useful in the treatment of nasal allergy in children . . . Personal experience reveals that children can acquire a technic for using the squeeze bottle themselves, without any adult assistance or fussing."*

1. Silbert, N. E.: GP, 8:15, Dec., 1953.

**WINTHROP LABORATORIES**
**DIVISION OF STERLING PHARMACEUTICALS PTY. LTD.**
I.A.56

## AN ALTERNATIVE TO LINCTUS HEROIN

"The control of the severe usually unproductive cough associated with tumours of the lungs and bronchi is a difficult therapeutic problem, for which hitherto, at least in this country, opiates including heroin have often been used. But American physicians have used alternatives for this purpose. Increasing interest is being shown in the antitussive properties of some of the new synthetic narcotics, especially in levorphan congeners such as dextrorphan and dextromethorphan. These substances, though they have no analgesic properties and are said not to produce addiction, have been found to be as effective as codeine and to cause no undesirable side-effects."

*Lancet*, 1955, ii, 1183.

". . . Dextromethorphan (known as 'Romilar') is said to have no side-effects, to maintain its efficiency over long periods, and not to induce addiction: it does not prevent the coughing up of phlegm or alter the consistence of the sputum, and it has no analgesic action."

*Lancet*, 1956, i, 565.

# 'ROMILAR'

TRADE MARK ROCHE

## DEXTROMETHORPHAN

**Packings: Syrup in bottles of 100 c.c. and 500 c.c. (15 mg. in 5 c.c.). Tablets (15 mg.), 20 and 200.**

**ROCHE PRODUCTS PTY. LIMITED, 1 BARRACK STREET, SYDNEY**

# LILLY FELLOWSHIP IN MEDICINE
# 1957 - 1958

***Eli Lilly and Company have been sponsoring fellowships in post-graduate medicine in various countries of the world since 1945. The aim of this programme has been to promote better understanding and to establish closer ties between members of the medical profession in the United States and other countries and to contribute to post-graduate medical education.***

***It has been decided that a fellowship should be offered to a suitable candidate within the Commonwealth of Australia, for the year 1957-1958.***

***Applications for the fellowship will close on July 31, 1957, and should be directed to the Secretary of the Lilly Fellowship Selection Committee, Dr. Ewen Downie, 111 Collins Street, Melbourne, Victoria.***

***The following information describes the terms governing the award of this fellowship, while further information and application forms may be derived directly from the Secretary.***

## FEATURES OF THE FELLOWSHIPS

**Duration**—The duration of the fellowship is twelve months from the time of arrival of the fellow in the United States.

**Fields**—The fellowship programme will support studies in internal medicine in general and its related fields, and other specialties, as follows:

Post-graduate work in internal medicine in general.
Diabetes and endocrinology.
Metabolism and nutrition.
Pulmonary diseases—diagnosis and treatment.
Hæmatology.
Allergy.
Infectious diseases, immunology, public health.
Dermatology.
Cardiology and cardiovascular diseases.
Renal diseases.
Clinical laboratory, bacteriology, parasitology.
Pharmacology and toxicology.
Gastro-enterology and diseases of the liver.
Pathology and cancerology.
Neurology and psychiatry.
Pædiatrics.

## FINANCIAL POLICIES

Each fellow will be granted a monthly stipend of $300.00, with round-trip expenses by air. As the Lilly fellowships are subject to income taxes, an extra stipend will be given to pay for the taxes.

All fees, tuition, books, and instruments will be borne from the stipend supplied to the fellows.

## SPONSORS

The fellows must be sponsored by any of the following: Dean of a medical school, an outstanding doctor, a local medical society, the educational board of a medical school for the selection of candidates for post-graduate study, or a committee organized locally among outstanding physicians or medical societies. In the latter case the Secretary of this committee will be responsible for corresponding with the Secretary of the Lilly Foreign Educational Fellowship Committee. The sponsor assumes no responsibility toward the Company, but he undertakes to make all the necessary arrangements with the American scientific institutions for the fellow's admission. These arrangements should be undertaken as soon as the sponsor is advised of the approval of the candidate by the Lilly Foreign Education Fellowship Committee. The sponsor is granted a period of two months in which to make these arrangements.

The selection of the candidates will be the responsibility of the sponsors, subject to the approval of the Lilly Foreign Educational Fellowship Committee and the university or U.S. medical institution where the fellow is to pursue his studies.

The sponsor will submit to the Fellowship Committee certificates attesting to the acceptability of the applicant, and this should be done not later than three months after the sponsor has been notified of his selection as a sponsor.

## APPLICANT REQUIREMENTS

Applicants for Lilly fellowships must be young physicians interested in self-improvement, who are active in the work being done by the universities or hospitals of which they are members, and who have shown interest in medical teaching and public health problems. Preferably the applicants should be doctors who have practised two or three years or who have acted in a professional capacity as assistant professors, chiefs of clinic, residents, etc., and who are assured of appointments in teaching institutions when they return.

The applicant must submit an application to the chairman of the Fellowship Committee, Dr. Ewen Downie, 111 Collins Street, Melbourne, Victoria, giving the following information:

1. Age (preferably, applicants should be 25-35 years of age).
2. Curriculum vitæ.
3. Letters of recommendation from two local, well-known physicians.
4. A summary of the work the applicant is engaged in.
5. Copies of medical publications of the applicant's authorship.
6. A short statement of the post-graduate studies the applicant plans to make.

Once a candidate has been approved by the Fellowship Committee the successful candidate will have a period of no more than two months in which to make the necessary arrangements, in co-operation with his sponsors and the Selection Committee, with the institutions in the United States for the place of study. The candidate must also make his trip arrangements within that time and full assistance can be provided.

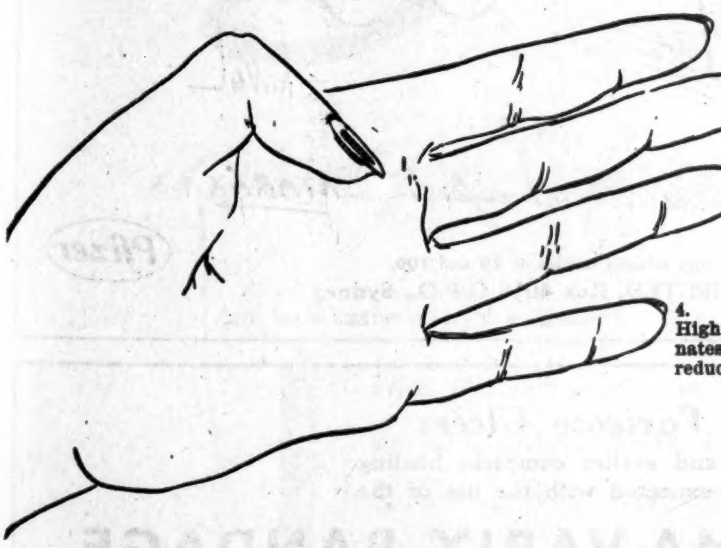
# SULPHADITAL

*the*

*Triplesulphonamide Mixture*

CONTAINING SULPHACETAMIDE

## SULPHADITAL EXHIBITS FOUR DISTINCT ADVANTAGES



1. Each component absorbed separately.

2. Each is acetylated and eliminated as if it were one substance.

3. A more rapid absorption because of the split dosage of each sulphonamide.

4. High solubility of the conjugated products eliminates the risk of concrement formation and reduces sensitivity.

These advantages make Sulphadital the sulphonamide of choice for such conditions as pneumococcal infections, staphylococcal infections (particularly in combination with certain antibiotics), streptococcal infections and many other infections for which sulphonamides have proved effective.

N.H.S. Item No. 158: This preparation is free to patients on prescriptions written under the N.H.S. Item No. 158.

## FAWNS & McALLAN

AUSTRALIA

*Irritabilité des enfants... ATARAX* *

Pfizer

Supplied: 10 mg. tablets, bottles of 20 and 100.

PFIZER PTY. LIMITED, Box 4016 G.P.O., Sydney

* Trade mark of CHAS. PFIZER & CO., INC.

*The Treatment of Varicose Ulcers*

**is considerably simplified, and earlier complete healing can be expected with the use of the**

# SIMA-VARIX-BANDAGE

- **Only one dressing every 3-4 weeks;**
- **"Ready for immediate use" presentation;**
- **Full length, firm, yet elastic support;**
- **Simanite impregnation against skin irritation, also promoting granulation.**

*are some of the advantages which have made SIMA-VARIX-BANDAGES indispensable for successful varicose ulcer treatment.*

Made in Australia by

**SIMANITE (A'sia) PTY. LTD., SYDNEY**

*Interstate distributors:*

WILLIAM PEARCE & CO. PTY. LTD.
Sydney, N.S.W. Tel. BM6129.

GRADWELL BROS.
Brisbane, Qld. Tel. B9739.

BRODERICK MacKINNON PTY. LTD.
280 King Street, Melbourne, Vic. Tel. MU3287.

MESSRS. PHARMACEUTICALS PTY. LTD.
93 York Street, Launceston, Tas. Tel. L'ton 2515.

ETHICO DISTRIBUTORS
Perth, W.A. Tel. BA5284.

# 'S-mez'

*Regd. Trade Mark*

## *is short for 'Sulphamezathine'*

*(Sulphadimidine B.P.)*

When prescribing, most doctors prefer short words. So to save your time, and because so much 'Sulphamezathine' is prescribed, we have registered the abbreviation 'S-MEZ'. You can now use this shortened version officially, knowing that 'Sulphamezathine' will be dispensed. 'Sulphamezathine'—or 'S-MEZ'; they both stand for sulphadimidine. But 'S-MEZ' is quicker to write than sulphadimidine.

Available under the National Health (Pharmaceutical Benefits) Regulations

Marketed in Australia by

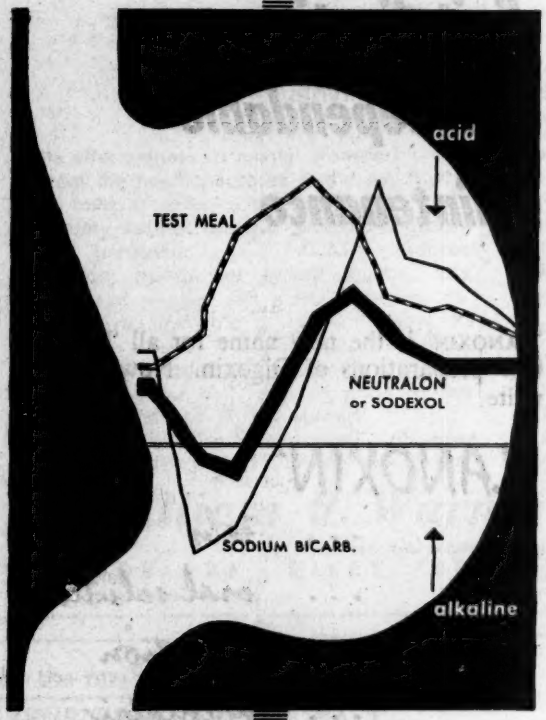
**IMPERIAL CHEMICAL INDUSTRIES OF AUSTRALIA & NEW ZEALAND LTD.**

A product of Imperial Chemical Industries Ltd. Pharmaceuticals Division, England

ICI

4954. M.ED. 1957. 980

"Perfect Control"
PROMINAL IN EPILEPSY




## For the hyperacid stomach

Prolonged neutralization of stomach acid by Neutralon or Sodexol. No excessive alkalinization at the start and no reactive hyperacidity

as powder **NEUTRALON**
**BELLADONNA - NEUTRALON**
tins of 100 g

as tablets **SODEXOL**
60 tablets of 1 g each

Schering

**SCHERING A.G. BERLIN · GERMANY**
Distributors: Schering (Pty.) Ltd., Sydney, Australia

## ORAL

**PBA**
**'Lanoxin' — Digoxin, 0.25 mg.**
*Bottles of 100, 500, 1,000 and 5,000 tablets.*

**PBA**
**'Lanoxin' — Oral Solution.**
*Bottles of 30 ml., containing 0.5 mg. Digoxin in each ml.*

## PARENTERAL

**PBA**
**'Lanoxin' — Injection Solution.**
For intramuscular or intravenous use without prior dilution.
*Ampoules containing 0.5 mg. Digoxin in 2 ml., in boxes of 6 and 100.*

## PÆDIATRIC

**'Lanoxin' — Paediatric Elixir.**
*Bottles of 2 fl. oz., containing 0.05 mg. Digoxin in each ml.*
Issued with dropper specially calibrated to ensure accurate measurement of dosages as low as 0.01 mg.

# *for prompt digitalisation and dependable maintenance*

'LANOXIN' is the new name for all 'B.W. & Co.' preparations of Digoxin. Now, simply write

## 'LANOXIN'

... tabs
... oral solution
... injection
... paediatric

to provide the safety and predictability afforded by the uniform potency, uniform absorption, brief latent period and optimum rate of elimination of this pure, stable, crystalline glycoside.

*for balanced digitalisation, always prescribe*

## 'LANOXIN'

BURROUGHS WELLCOME & CO. (AUSTRALIA) LTD., SYDNEY, N.S.W.

# A new product

# PACATAL*

n-Methyl-piperidyl-(3)-methyl-phenothiazine

a powerful yet safe tranquillizing drug.

Its effectiveness in mental disorders range from the psychoneuroses to the psychoses. In mild or severely disturbed states . . . anxiety, restlessness, excitement and abnormal behaviour . . . PACATAL reduces tension, makes the patient quieter, less confused — but still alert, objective, co-operative amenable to psychotherapy. In addition Pacatal is a potentiator of anaesthetics and sedative-hypnotics. It is a valuable drug for both premedication of the patient and use during surgery.

PACATAL can be administered with complete confidence for it is of very low toxicity and uniquely free from such troublesome side-effects as skin rashes, jaundice, Parkinson symptoms, orthostatic collapse and tachycardia. As a further safeguard, PACATAL is rapidly absorbed and quickly eliminated, thus ensuring against cumulative dangers.

PACATAL is available in tablets for oral administration and ampoules for parenteral use.

Tablets; 25 mg. in bottles of 100 and 500. Ampoules; 2 c.c. (25 mg. /c.c.) in boxes of 6 and 100.

* Reg. T. Mark

**William R. Warner & Co. Pty. Ltd.**

SERVING THE MEDICAL PROFESSION SINCE 1856

508-528 RILEY STREET, SYDNEY, N.S.W.

TELEPHONE: MX 2355 TELEGRAPH: "QUICKPILL"



**To the medical profession:**

**SYRUP EPHEDRAMINE No. 1**

**SYRUP EPHEDRAMINE No. 2**

*for*

## *Respiratory Tract Therapy*

*We are pleased to announce the introduction of two improved products to replace "Syrup Ephedramine-Lennon".*

**SYRUP EPHEDRAMINE No. 1**

This product remains the same as the original except that the morphine content has been omitted. This step has been taken to comply with modern trends of asthma treatment.

**SYRUP EPHEDRAMINE No. 2 (Iodine-free)**

This product is the same as Syrup Ephedramine No. 1 except that the potassium iodide has been omitted to facilitate the treatment of asthmatic patients exhibiting an iodine idiosyncrasy.

We feel that these products mark a considerable advance in respiratory tract therapy and will prove of valuable assistance to the physician. They are confidently offered for your consideration.

*Sample bottles and literature will be forwarded gladly upon request.*

**HUNTER LABORATORIES LTD.**

formerly known as CLEVELAND S. LENNON LTD.

NEWCASTLE

Sydney Office: 9 Norton Street, Ashfield. UA6640.

PREPARED, WITHOUT SUSPENDING AGENT . . .

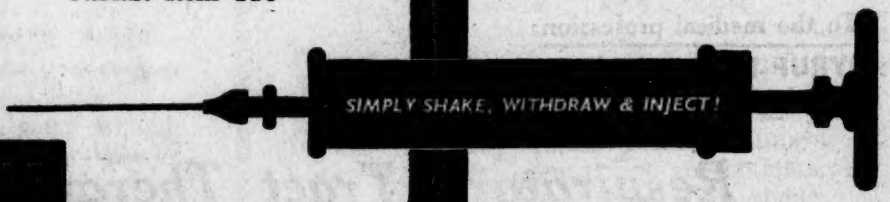
# *Cilicaine

SUSPENSION

*Cilicaine Suspension . . .*
*a stable, buffered*
*aqueous suspension*
*of micro-fine procaine*
*penicillin G (300,000 u/ml.).*
*Available in 1,500,000 and*
*900,000 unit vials*

**N.H.S. Item 110**

*Cilicaine Suspension should be your "first choice" in penicillin therapy, because it is now available*
*WITHOUT SUSPENDING AGENT*
*WITH A LUBRICANT.*
*Cilicaine Suspension offers . . .*
*a water mobile suspension*
*easiest injection . . . with the*
*advantages of your own syringe.*
*Pain-free injection . . . absence of*
*inert suspending material.*
*Highly satisfactory absorption*
*and blood levels.*




* Aqueous Procaine Penicillin

MANUFACTURED BY SIGMA COMPANY LIMITED, MELBOURNE.

Interstate distributors:
The Wholesale Drug Co. Ltd., Sydney.
Queensland Druggists Ltd., Brisbane.
Southern Drug Co. Ltd., Adelaide.
Rumbles Ltd., Perth.

MAKERS OF FINE PHARMACEUTICAL PRODUCTS

SIGMA

SCS-7a

As the magnet attracts steel...

# KALOPECTIN

adsorbs and removes
bacteria, toxins and other irritants
in simple and complex
DIARRHOEAS

*Kalopectin coats and protects irritated intestinal mucosa and consolidates the stool to normal consistency.*

| KALOPECTIN NO. 1 | | KALOPECTIN NO. 2 | |
|---|---|---|---|
| Contains in each fl. oz. | | Contains in each fl. oz. | |
| COLLOIDAL KAOLIN | 6 gm. | COLLOIDAL KAOLIN | 3 gm. |
| APPLE PECTIN | 0.3 gm. | PHTHALYL-SULPHACETAMIDE | 4 gm. |
| | | APPLE PECTIN | 0.3 gm. |

Issued in bottles of 4, 8 and 40 fl. ozs.
Obtainable from all pharmacies

PALATABLE AND STABLE SUSPENSIONS.

***May be used alone or as prescription vehicles.***

Physicians' samples and literature available on request.

AN AUSTRALIAN-MADE ETHICAL BY

Charles McDonald PTY. LTD.

MAKERS OF PHARMACEUTICAL SPECIALTIES

SYDNEY, AUSTRALIA

*...cause it combines all* **3**

***Pectin—enhances hydrophilic properties***

*Colloidally dispersed in a special adsorbent* ***alumina gel***

***Purified Kaolin***

# KAOMAGMA with PECTIN

is effective in Control of Diarrhoea

Relief is quick . . . Kaomagma with Pectin soothes and protects inflamed intestinal mucosa. Cramps and distention are promptly relieved.

**Consolidates stools . . . checks fluid loss . . . restores patient's comfort.**

**Dosage:** At onset give two tablespoonfuls in water; then 1 tablespoonful after every loose bowel movement.

***Presentation:*** *Bottles of 6 and 12 fl. oz.*

*Wyeth*

*Wyeth* INTERNATIONAL LIMITED (Inc. in U.S.A.), P.O. Box 148, Parramatta, N.S.W.
'Phone: YL7141-42

Koop/1/M/57

*for greater antibiotic absorption —*

*— faster broad-spectrum action*

*new*

# ACHROMYCIN V

Lederle

**Tetracycline Buffered with Sodium Metaphosphate**

*a new improved form of a clinically proven antibiotic*

ACHROMYCIN V combines the well-known antibiotic, tetracycline, with metaphosphate to provide greater and more rapid antibiotic absorption in the intestinal tract. This increased absorption is evidenced by significantly higher blood levels and by an increased rate of urinary excretion of the ingested drug.

*chemically conditioned for greater clinical efficiency*

The chemical structure of ACHROMYCIN remains unaltered. However, its tetracycline action is intensified. Chemically conditioned with metaphosphate, ACHROMYCIN V places a newer, more effective therapeutic agent in the hands of the physician. ACHROMYCIN V is indicated in all conditions indicated for ACHROMYCIN Tetracycline. The recommended dose remains the same, one gramme per day for the average adult.

Available: Bottles of 16 and 100 capsules.

Each capsule (pink) contains:

Tetracycline equivalent to tetracycline HCl, 250 mg.
Sodium metaphosphate, 380 mg.

Dosage: 6-7 mg. per lb. body weight per day for children and adults.

**Available as a Pharmaceutical Benefit (Restricted Drug)**

**ACHROMYCIN V — A LEDERLE PRODUCT**

***Distributed throughout Australia by ALL D.H.A. HOUSES***

# *For Teletherapy with Cobalt 60*

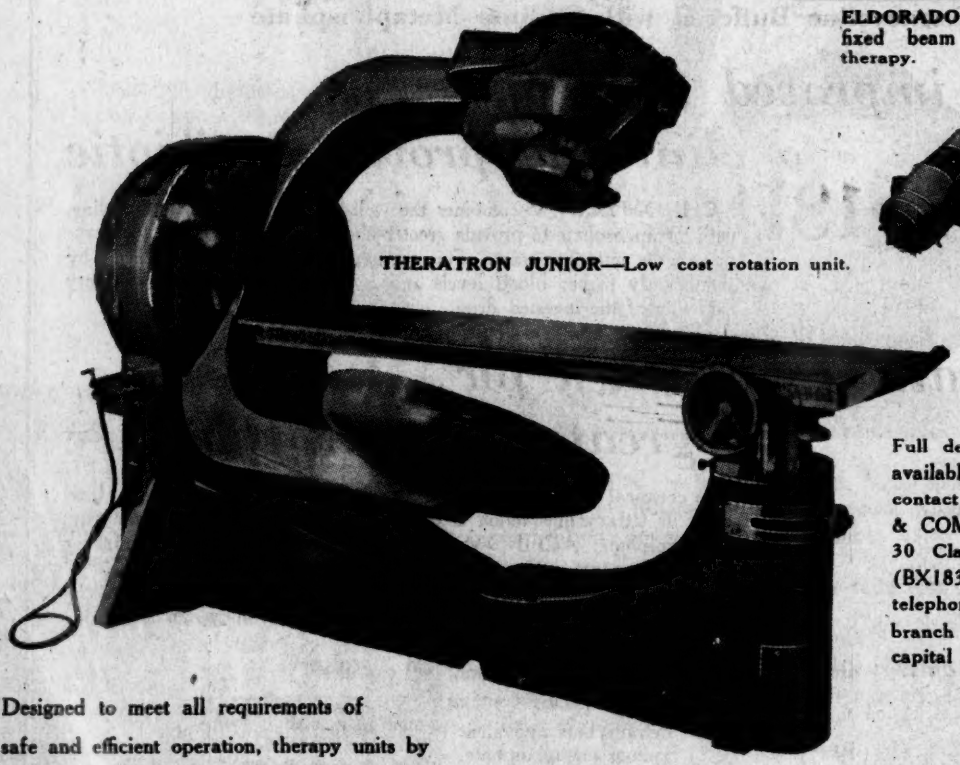
## ATOMIC ENERGY OF CANADA LTD.

Provides beam therapy units backed by unrivalled experience of developments on this expanding medical frontier. Over 50 such units are now in use at progressive medical centres the world over.

**THERATRON**—Kilocurie unit designed for ease and efficiency in moving beam therapy techniques.

**ELDORADO MODEL** — For fixed beam or multiportal therapy.

**THERATRON JUNIOR**—Low cost rotation unit.



Full details of all units are available on request. Please contact agents — SWIFT & COMPANY LIMITED, 26-30 Clarence Street, Sydney (BX1831) — or check your telephone directory for the branch office in your nearest capital city.

Designed to meet all requirements of safe and efficient operation, therapy units by Atomic Energy of Canada Ltd. are now readily available for installation.

**Head Office: 26-30 CLARENCE STREET, SYDNEY**

**Also at Melbourne, Brisbane, Adelaide, Perth, Wellington and Auckland (N.Z.)**

*At the service of Industry and Science since 1897.*

**SWIFT**
**AND COMPANY LIMITED**

S573

# Consolidated attack...

# 'Distaquaine' V Sulpha tablets

'DISTAQUAINE' V SULPHA offers a new and reliable form of penicillin/sulphonamide therapy convenient to both practitioner and patient.

This balanced combination of two rapidly and efficiently absorbed sulphonamides with acid-stable 'Distaquaine' V provides, for the first time, the effectiveness of treatment with sulphonamides and penicillin in a single oral preparation.

SOLE IMPORTERS

**BRITISH DRUG HOUSES (AUSTRALIA, PTY.) LTD., 250, Pitt Street, Sydney**

*Manufactured in England by:*

'DISTAQUAINE' V
*for reliable penicillin levels*
SULPHADIMIDINE AND SULPHAMERAZINE
*for enhanced antibacterial effect*

*Each tablet contains:*

| | |
|---|---|
| PENICILLIN V | 60 mg. |
| SULPHADIMIDINE | 0.30 gm. |
| SULPHAMERAZINE | 0.14 gm. |

DOSAGE

*Adults:* Initial dose of two tablets followed by one or, in specially serious cases, two tablets six times a day at not more than four-hourly intervals.
*Children:* Half the adult dose.
*Infants:* Quarter the adult dose.

PACKS: Bottles of 30 and 200 tablets

THE DISTILLERS COMPANY (Biochemicals) LIMITED • LONDON & LIVERPOOL
*owners of the trade mark 'Distaquaine'*

FPO 2/57A

Bacterial Ballads
no 2
As I set out on a tour of infection
With a cargo of sickness for all humankind,
I spied a young germ in the depths of dejection,
He looked up and saw me, and plaintively whined:
"Turn back, brother germ, please abandon your mission,
This place spells disaster—believe me, I know.
For the people are armed with a deadly munition
Called Wright's Coal Tar Soap. We're defeated—let's go!"
WRIGHT'S COAL TAR SOAP
Ideal for Toilet, Bath and Nursery.
Wright's COAL TAR SOAP
Awarded for 50 years the Certificate of Merit of the Royal Institute of Public Health and Hygiene.

**Australasian distributors: Commonwealth and Dominion Agencies, Kingsgrove, Sydney.**

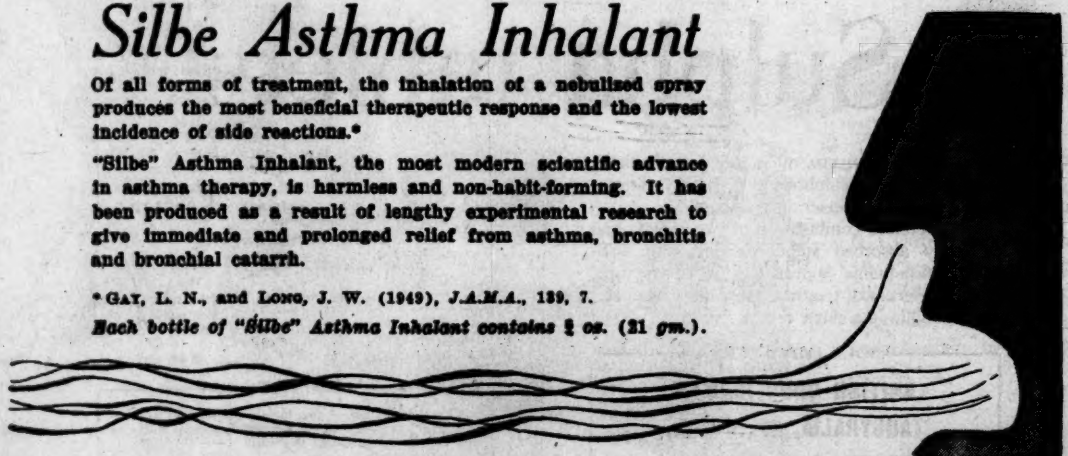
# *Silbe Asthma Inhalant*

**Of all forms of treatment, the inhalation of a nebulised spray produces the most beneficial therapeutic response and the lowest incidence of side reactions.***

**"Silbe" Asthma Inhalant, the most modern scientific advance in asthma therapy, is harmless and non-habit-forming. It has been produced as a result of lengthy experimental research to give immediate and prolonged relief from asthma, bronchitis and bronchial catarrh.**

* GAY, L. N., and LONG, J. W. (1949), *J.A.M.A.*, 139, 7.

***Each bottle of "Silbe" Asthma Inhalant contains* ½ *oz.* (21 *gm.*).**



**FORMULA**

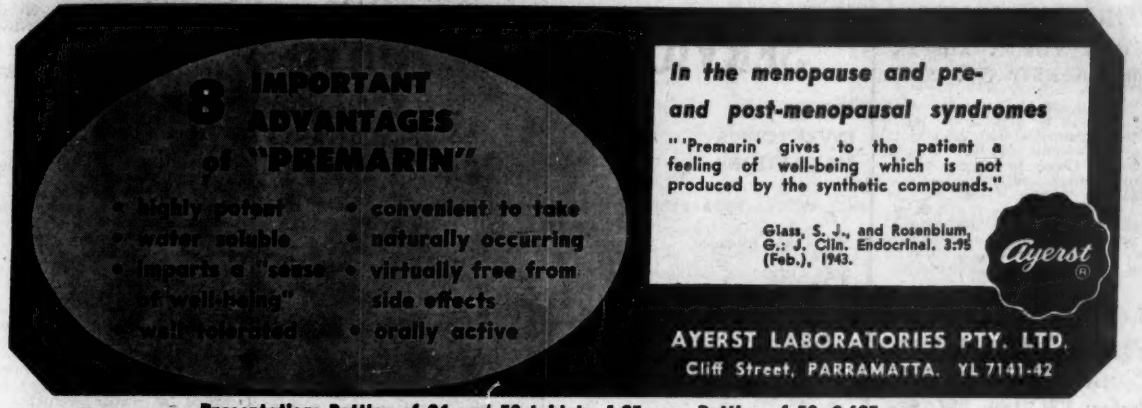
| | |
|---|---|
| **Papaverine Hydrochloride B.P. 0·95% w/v** | **Chlorbutol B.P. ..... 1·00% w/v** |
| **Adrenaline B.P. ..... 0·50% w/v** | **Hyoscine Hydrobrom. B.P. 0·05% w/v** |
| **Atropine Methonitrate B.P.C. 0·125% w/v** | **Glycerin B.P. ..... 35·00% v/v** |
| **Pituitary Liquid Extract B.P. 20·00% v/v** | **Distilled Water B.P. to 100% v/v** |

SILBE

*Literature and samples from—*

**E. H. FLORANCE, BOX 3122 G.P.O., SYDNEY**

MANUFACTURED BY SILTEN LTD., HATFIELD, HERTS., ENGLAND


8 IMPORTANT ADVANTAGES of "PREMARIN"
• highly potent
• water soluble
• imparts a "sense of well-being"
• well tolerated
• convenient to take
• naturally occurring
• virtually free from side effects
• orally active
In the menopause and pre- and post-menopausal syndromes
"'Premarin' gives to the patient a feeling of well-being which is not produced by the synthetic compounds."
Glass, S. J., and Rosenblum, G.: J. Clin. Endocrinal. 3:75 (Feb.), 1943.
Ayerst
AYERST LABORATORIES PTY. LTD.
Cliff Street, PARRAMATTA. YL 7141-42

**Presentation: Bottles of 24 and 50 tablets, 1.25 mg. Bottles of 50, 0.625 mg.**


OUNT MORGAN HOSPITALS BOARD, QUEENSLAND.

PPLICATIONS are hereby in- d for a Junior Resident Medical cer for the Mount Morgan spital.

alary range: first year ex- ence £1266 10s. per annum, nd year experience £1421 10s annum.

subsidy of £350 will be paid Mount Morgan, Limited, after lve (12) months' continuous rice at the hospital.

artly furnished house provided, ther with free fuel, light and ter.

pplications, giving full par- lars of age, experience, marital us, etc., and stating earliest available for duty, together h references, should be ad- ssed to the Secretary, P.O. Box Mount Morgan, Queensland.

1948 GRADUATE, four years' general practice experience in tralia, two years' hospital ex- ence in England, and one year's pital experience in the United tes of America, returning to tralia end of 1957, seeks stantship with view in general ctice, Sydney or environs. Reply 98, c.o. this office.

ART OR FULL TIME LOCUM REQUIRED BY FEMALE ADUATE. Experienced general ctice. Own car. Sydney area. ly No. 74, c.o. this office.

FOR SALE.

Brisbane city practice. Good residential suburb. Income £5000 p.a. Rent of surgery £5 5s. Goodwill £2650.

Country solo practice. Income £7500. Goodwill £3000. Property.

Country solo practice. Income £4500. Goodwill £2500. Property.

DAVID W. REID,
"Wickham" House", Wickham Terrace, Brisbane.

ASSISTANT WANTED with view to partnership in well-established group practice in north coast centre with base hospital facilities. Experience necessary in obstetrics and pædiatrics. Car essential. Protestant preferred. Salary from £1800 p.a., according to age and experience. £5 per week car allowance. Accommodation arranged. Reply No. 99, c.o. this office.

TYPIST, experienced in medical and scientific phraseology, available for home typing service. Theses a speciality. UJ 2319 (Sydney).

GENERAL PRACTICE WANTED, Sydney suburbs. Preferably solo. Replies to No. 95, c.o. this office.

LOCUM AVAILABLE, occasional week-ends and night surgeries, Sydney area. Own car. Reply No. 104, c.o. this office.

BALMAIN AND DISTRICT HOSPITAL, N.S.W.

APPLICATIONS are invited for a resident medical officer to act as a Registrar in the maternity section which is recognized under the regulations governing the Diploma in Gynæcology and Obstetrics. Salary £1221 per annum.

Apply H. W. SIMPSON, Chief Executive Officer and Secretary, Balmain and District Hospital, Booth Street, Balmain, Sydney.

FAIRFIELD DISTRICT HOSPITAL, N.S.W.

HONORARY MEDICAL STAFF.

APPLICATIONS on special forms, obtainable on request, closing in the office of the undersigned on 20th July, 1957, are invited for the following honorary medical staff appointments to the above hospital in accordance with the hospital relevant by-laws and rules:

Honorary Relieving Assistant Obstetrician (2 positions).

Further particulars on reques: from JAMES F. LIDDY (Secretary), Fairfield District Hospital, Fairfield, N.S.W.

TO LET, three large rooms nearing completion. Suitable specialist. Busy shopping centre. 579 Sydney Road, Seaforth, or ring XJ 5957 (Sydney).

LEONORA DISTRICT HOSPITAL, LEONORA, W.A.

A vacancy exists for a Resident Medical Officer for the Leonora District Hospital, Leonora, W.A. (Government subsidized). Guaranteed minimum salary from fund £2300 per annum, plus the right of private practice, including surgery, midwifery (approximately 40 per annum), and workers' compensation cases.

New unfurnished residence now in process of being built, with septic system, situated near hospital, is available at a weekly rental of £3, which includes free firewood and water. A charge of £4 per week is made for the use of surgery.

Situation becomes vacant on 15th August, 1957. Applications from fully qualified practitioners will close with the Chairman, Leonora Hospital Board, Post Office Box 37, Leonora, W.A., on 10th July, 1957.

Further particulars can be obtained from the Secretary of the Board at the same address.

F. W. BOWKER, 28 LONGUEVILLE ROAD, LANE COVE, SYDNEY, JB 1314.

Wanted to purchase, E.C.G.'s (direct writers) urgently. Also sterilizers and shockproof X-ray units.

For sale, new examination couches from £19 10s., Neville-Barnes obstetric forceps, stainless steel, £10.

## MEDICAL AGENTS

### PRACTICES FOR TRANSFER LOCUMS, ASSISTANTS, ETC.

1. N.S.W. Old-established solo unopposed practice in Southern Highlands. G.C.T. over £6000. District hospital. Goodwill £1100. Brick residence of three bedrooms with main furnishings and floor coverings, £3500. Terms.

2. Sydney. Substantial, old-established practice in good residential district. Gross cash about £7500. Suite of rooms leased. No residence. Goodwill £5500.

**All Enquiries Confidential.**

**GOYDER, SON & CO.**

**11c Castlereagh Street, Sydney**

**Telephones: BW 7149, BW 7828**

**After Hours: JJ 3665**

**Cables and Telegrams: "MEDANREAL, Sydney"**

The name of Goyder has been Associated with Medical Agency since 1902.

---

BURNIE GENERAL HOSPITAL, BURNIE, TASMANIA.

RESIDENT MEDICAL OFFICER.

APPLICATIONS are invited for this position. Salary £1328 p.a. Good quarters. General, midwifery, and a busy casualty service. A little over an hour's flight from Melbourne. Fare refunded on arrival. Inquiries invited.—JNO. S. CAMBRIDGE, Secretary.

---

NON-SECTARIAN 1946 SYDNEY GRADUATE NEEDS ASSISTANT in mildly tropical Queensland east coast city of over 40,000. Comprehensive hospital cultural, school, etc., facilities. Living cost shames southern cities. £50 p.w. including allowances. Partnership decision in three months. Easy terms. Reply No. 15, c.o. this office.

---

**COLLECTORS**

**"JAYS" of Melbourne**

**We collect overdue accounts within the State, throughout Australia and Overseas.**

**Please post your list to**

**JAYS AGENCY,**

**220 Collins St., Melbourne,**

**or 'phone Central 1031-2058 and we will call.**

---

# SERVICE for DOCTORS

**PRACTICES**
**INVENTORIES**
**VALUATIONS**

WATSON VICTOR LTD

**LOCUMS**
**ASSISTANTS**
**PARTNERSHIPS**

**• CONFIDENTIAL SERVICE •**

**No. 1365: Sydney.**

Solo practice in good residential area taking £9000. Goodwill £4500. Good property with all amenities, £5600. Vendor will accept terms. A really good opening to enter a well-established practice.

**No. 1367: North-west slopes, N.S.W.**

Solo practice taking £6000. Goodwill £3000. Very nice three-bedroom timbered residence, £3500. Liberal terms considered. Good town. Good hospital. Well-known grazing area.

**No. 1368: North-west, N.S.W.**

Solo opposed practice taking £6227. Goodwill £3000 cash. Spacious timbered residence in nice garden, £4500, on good terms. Most modern hospital and scope for surgery.

**No. 1369: N.S.W. Hunter Valley.**

Solo practice taking £7000. Goodwill £3250. Pleasant house having good rooms. New surgery block. Property well situated. £3250. Terms available.

**No. 1370: N.S.W. Southern slopes.**

Solo practice. Ideal for practitioner who seeks a pleasant country practice. Taking £4000. Good hospital. Two-storey stone house in good grounds. Goodwill and property £5000. Bank overdraft can be arranged. Well worth considering.

**No. 1371: N.S.W. Riverina.**

Partnership practice taking £14,500. Ideal for two friends or husband and wife. Goodwill £4000. Well-equipped hospital and in good location. Property of brick, £5500. Another residence available for friend, £2950. Vendors proceeding overseas. Attractive terms considered.

*Particulars in confidence.*

**WATSON VICTOR LIMITED** 9 Bligh Street, Sydney BW4433

**Also at Brisbane, Melbourne, Perth, Adelaide, Newcastle, Hobart, Launceston**

---

BALMAIN AND DISTRICT HOSPITAL, N.S.W.

APPLICATIONS are invited for the position of Senior Resident Medical Officer at the Balmain and District Hospital. Salary £1221 per annum. Apply, stating age, experience and with copies of references, to H. W. SIMPSON, Chief Executive Officer and Secretary, Booth Street, Balmain. Telephone WB 2013.

---

A 1953 GRADUATE, two years' hospital, two years' G.P. experience, wants assistantship with view, North Shore, Sydney. Car. Accommodation not required. FX 4960.

---

ASSISTANT, view partnership twelve months, wanted to join group practice of five, forty miles from Sydney. Obstetrical and surgical experience desired. £2000 p.a., plus house, plus £5 per week car allowance. Must be married. Reply No. 83, c.o. this office.

---

MEDICAL PRACTICE TO LEASE, western suburbs, Sydney. Takings £4000. Two well-furnished rooms, very good position. Reply No. 105, c.o. this office.

---

EXPERIENCED G.P., Australian male, available for locums (live out), eastern suburbs, Sydney, from 1st August, 1957, to 1st January, 1958 (teaching hospital, six years solo practice). Reply No. 107, c.o. this office.

---

MOUNT ISA HOSPITAL BOARD, QUEENSLAND.

MEDICAL OFFICER.

APPLICATIONS are invited for the position of Medical Officer, the Mount Isa Hospitals Board. To be resident in Mount Isa for Mount Isa and Camooweal districts. (A right of private practice.) Salary at rate £2045 per annum plus current wage adjustments of £36 10s, district allowance of £75 per annum. Appointee may accept fees for certificates issued for pensions and insurance examinations. In addition, Mount Isa Mines Ltd. will pay a bonus of £265 for each completed year of satisfactory service. Four weeks' annual leave on full pay. Special taxation zone allowance of £180 per annum applies in this area. If the appointee provides a motor vehicle which is desirable, Mount Isa Mines Ltd. will pay an allowance of £15 per month to maintain it.

A furnished house with electric light, water and sewerage will be provided free. Applicants are required to furnish particulars of age, marital state, qualifications and experience and war service, if any. Daily average in-patients, Mount Isa Hospital approximately 50.

Applications close with Secretary on 22nd July, 1957, and the successful applicant will be required to commence duty on or about August, 1957. For further particulars apply to Secretary, Box 63, P.O., Mount Isa, Queensland.

---

AN EXPERIENCED PRACTITIONER with car available for locum tenens or part-time week-ends, holidays, etc. Suburban (north side) preferred. XM

---

INDUSTRIAL PRACTICE, in easy reach of Sydney, requires Assistant, view partnership. Salary £50 per week plus all expenses. Suit young energetic man with G.P. experience and limited finance. Reply No. c.o. this office.

---

**SURGICAL INSTRUMENTS**

**MEDICAL BOOKS**

**HOSPITAL EQUIPMENT**

**Consult**

**HANNAMS, RAMSAY PTY. LTD.,**

**124 Castlereagh Street, Sydney.**

**'Phone: MA 5838.**

---

**BRITISH MEDICAL AGENCY OF QUEENSLAND PTY. LTD.**

**89 L'ESTRANGE TERRACE, KELVIN GROVE, W.1, BRISBANE.**

SALE OF PRACTICES
LOCUM TENENS
INVESTMENTS
FIRE INSURANCE
ACCIDENT INSURANCE
'Phone: S. N. COBBOLD, Manager, B 1855.

PURCHASE OF PRACTICES
PARTNERSHIPS
INDENTS
LIFE ASSURANCE
ENDOWMENT ASSURANCE
Telegrams: "Medicine", Brisbane.

## DICAL PRACTICES

gy. Solo practice, established years, in residential area, ging over £8000 with mid- y and surgery. Transferable al appointments. Good house surgery attached for sale at , and vendor would be pre- to rent. Goodwill £4500 and al terms by arrangement.

astle. Solo lock-up practice ging £8500. Established over ars. Excellent hospital facili- and some appointments trans- le. Modern surgery building ental of £5 p.w. or purchase. will £5000 on £1500 deposit, over five years.

## CHARD THOMSON & CO. PTY. LTD.

**Castlereagh Street, Sydney ween Bathurst and Park ts, T. & G. Building, on street level).**

2561. BM 2562.

**After hours:**

L. Hanrahan: FF 3343.

G. Garden: XJ 2500.

**erous positions available for cum tenens and assistants.**

---

### MORE BASE HOSPITAL, N.S.W.

PPLICATIONS are invited for position of Senior Resident cal Officer, with salary and itions according to the latest rmination of the Hospitals mission of N.S.W. (Present from £1221 p.a., according to rience.) Quarters for single ons only.

pplicants, who must have had east one year's hospital ex- nce, should give their full e, age, qualifications and ex- nce, together with copies only any references held.—J. O. KE, Secretary.

---

### EDICAL OFFICERS (MALE), DEPARTMENT OF PUBLIC HEALTH.

lary £1855, range £2325. Com- cing rate according to quali- ions and experience. Duties include medical examination ntrants to the Public Service relief in various branches as sary. Preference will be for transfer to various ions of the Department as ible vacancies occur. Appli- must be registered medical titioners and must have at two years' experience after uation. Apply PUBLIC SERVICE D, 19 O'Connell Street, Sydney, 12th July, 1957. For informa- 'phone BL 1779.

---

### RADUATE (1952) DESIRES WORK, Sydney eastern rbs, in mornings or on week- Post-graduate study limits table time. FY 1626.

---

### POST-GRADUATE STUDY BY CORRESPONDENCE FOR ALL BRITISH AND AUSTRALIAN MEDICAL EXAMS.

Diploma in Anæsthetics; Diploma in Psychological Medicine; Diploma in Ophthalmology; Diploma in Radiology; Diploma in Laryngology; Diploma in Child Health; F.R.C.S.Eng., and all Surgical Examinations; M.R.C.P.Lond., and all Medical Examinations; M.D. Theses of all Universities; Courses for all Qualifying Examinations. Complete Guide to Medical Examinations sent free on application. Applicants should state in which qualification they are interested. Address: Secretary, Medical Correspondence College, 19 Welbeck St., London, W.1.

---

### SOUTH-WEST NEW SOUTH WALES.

An opportunity exists for a capable young practitioner with adequate surgical experience for general practice as a third partner following a six-month trial period.

The practice is a rapidly expanding self-contained clinic with short-wave, X ray and E.C.G., with no night surgeries.

A modern large hospital with all facilities is present in a progressive town.

No deposit will be required and finance will be arranged over five years. Housing can be arranged. Salary £50 per week plus car allowance.

Inquiries to No. 110, c.o. this office.


***The Printing House***

***for***

**Professional Stationery**

**Scientific Publications**

**Reports**

**And all classes of Printing**

**Australasian Medical Publishing Co. Ltd.**

**Seamer Street, Glebe, Sydney**

**Telephone MW 2651-2-3**


---

### "THE MEDICAL JOURNAL OF AUSTRALIA."

### APPOINTMENT OF ASSISTANT EDITOR.

An Assistant Editor is required for "The Medical Journal of Australia". The appointment will be full time, and the appointee will be required to serve a probationary period of six months. Applicants should state their age, and give details of their education at school and university and of their post-graduate experience. The initial salary offered will be £2250 per annum with superannuation.

Applications, which will close on July 31, 1957, should be forwarded to The Secretary, Australasian Medical Publishing Company Limited, The Printing House, Seamer and Arundel Streets, Glebe, New South Wales.

---

### LECTURER IN THE LIVERPOOL SCHOOL OF TROPICAL MEDICINE, ENGLAND.

APPLICATIONS are invited for the post of Lecturer in the School in some branch of tropical medicine, including experimental medicine, clinical medicine, parasitology, entomology or hygiene. The lecturer will be a member of the home establishment, but will be expected to serve in the tropics in a selected station or in a university or similar institution.

The appointment will be made for five years in the first instance. The salary will be within the range of that for Lecturer, Grade II (clinical) with F.S.S.U. allowances, the starting point being determined by qualifications and experience. It ranges from £1000 to £1750 per annum, but the scale is at present under review.

Applicants must be medically qualified and should have had previous experience in their chosen field. Experience in the tropics is desirable but not essential.

The successful applicant will be expected to take up his duties as early as possible during the session commencing October, 1957.

Applications, including the names of two referees, should be forwarded to the Administrative Secretary, Liverpool School of Tropical Medicine, Pembroke Place, Liverpool, 3, by August 31, 1957.

Further details may be obtained from the Administrative Secretary.

---

YOUNG MARRIED WOMAN, four years' nursing training (Army), with considerable experience, book-keeping, receptionist and typing, would like position in doctor's surgery. In or near city preferred. Please ring WA 1378, Sydney (Mrs. Harrison).

---


WILLIAM PEARCE

**MEDICAL PRACTICES**

**Locums and Assistants available.**

No. 422. N.S.W. Situated on coast within easy reach of Sydney. Opposed general practice taking £4900. Excellent hospital facilities. Goodwill £2000. Modern brick residence for sale below V.G. Finance available.

No. 436. North Western Slope, N.S.W. Opposed solo practice established 60 years. District hospital. Average G.C.T. £5000, steadily increasing. Fifty mids. Goodwill £2000. Brick residence of 13 rooms, £4500. Terms, half cash.

No. 437. Western suburbs, Sydney. A soundly established general practice. Opposed. Gross takings average £7260. Owner leaving general practice. Excellent prospects of further development. Goodwill £3250. Large two-storey brick residence in splendid position to purchase.

No. 439. Sydney suburban. An opposed solo practice established over 35 years within five miles of G.P.O. taking (last year) £9349. Excellent opening for surgeon. Goodwill £4500. Brick residence and professional rooms £5600.

WILLIAM PEARCE AND CO. PTY. LTD
LICENSED REAL ESTATE AND BUSINESS AGENTS
149 CASTLEREAGH STREET, SYDNEY
Phones [illegible]


---

### BRISBANE SUBURBAN PRACTICE FOR SALE.

Share partnership practice established 50 years. Situated in suburban shopping centre. Time off. No night surgeries. Share of net income £4400. Replies to No. 109, c.o. this office.

---

RADIOLOGIST: Assistant Radiologist wanted for Melbourne practice with a view to future partnership. Salary £2700 per annum, the successful applicant to provide his own car. Apply No. 106, c.o. this office.

---

RADIOLOGIST WANTED. D.D.R. (or equivalent). Partner, lessee, assistant, locum (any period). £70 weekly. N.S.W. Reply No. 108, c.o. this office.

---

AUSTRALIAN GRADUATE, 1952, F.R.C.S., England, married, own car, G.P. experience, requires locum (N.S.W.) for three to six months from 14th July, 1957. Reply No. 103, c.o. this office.

# VITAMIN B-COMPLEX DEFICIENCIES

## MULTI-B

**EACH TABLET CONTAINS:**

| | |
|---|---|
| VITAMIN $B_1$ | 2·0 mgm. |
| RIBOFLAVIN | 2·5 mgm. |
| NIACINAMIDE | 20·0 mgm. |
| PYRIDOXINE HCl | 0·2 mgm. |

## MULTI-B PLUS

**Each Tablet contains the Multi-B formula with 2·5 mg. Dextro-Amphetamine Sulphate**

B-COMPLEX VITAMINS WITH
CENTRAL-NERVOUS-SYSTEM
**STIMULATION**

## MULTI-B
### WITH PHENOBARBITONE

**Each Tablet contains the Multi-B formula with ¼ gr. Phenobarbitone.**

B-COMPLEX VITAMINS WITH
CENTRAL-NERVOUS-SYSTEM
**SEDATION**

## MULTI-B FORTE

**EACH TABLET CONTAINS:**

| | |
|---|---|
| VITAMIN $B_1$ | 5·0 mgm. |
| RIBOFLAVIN | 4·0 mgm. |
| NIACINAMIDE | 30·0 mgm. |
| PYRIDOXINE HCl | 0·5 mgm. |
| VITAMIN C | 30·0 mgm. |

**A HIGH POTENCY VITAMIN B-COMPLEX AND VITAMIN C COMBINATION**

SYDNEY G.P. AUSTRALIA

7817


Printed and published by [illegible] MEDICAL PUBLISHING COMPANY LIMITED at the registered office of the company, The [illegible], Seamer Street, Glebe, Sydney, New South Wales.